

SEARCH REQUEST FORM

4-27

Examiner # (Mandatory): _____ Requester's Full Name: Niranaz S. Bas.Art Unit 1646 Location (Bldg/Room#): 10E17 Phone (circle 305 306 308) 308 9435Serial Number: 08/1983,474 Results Format Preferred (circle): PAPER DISK E-MAILTitle of Invention Alpha-Beta C4BP-Type Recombinase Heterodimers, ProteinsInventors (please provide full names): David Klatzmann & Jacques GherEarliest Priority Date: 6/30/1998

Keywords (include any known synonyms registry numbers, explanation of initialisms):

Search Topic:

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| | <input checked="" type="checkbox"/> Other (specify) <u>DNA CompuGen</u> | |

* WELCOME TO THE *
* U.S. PATENT TEXT FILE *

=> e klatzman, david/in

| E# | FILE | FREQUENCY TERM |
|-----|-------|--------------------------|
| E1 | USPAT | 1 KLATZKA, JOSEPH H/IN |
| E2 | USPAT | 1 KLATZKOW, LEIF/IN |
| E3 | USPAT | 0 -> KLATZMAN, DAVID/IN |
| E4 | USPAT | 2 KLATZMANN, DAVID/IN |
| E5 | USPAT | 1 KLAUBA, BRUCE/IN |
| E6 | USPAT | 4 KLAUBER, GERALD/IN |
| E7 | USPAT | 1 KLAUBER, MARK/IN |
| E8 | USPAT | 16 KLAUBER, ROBERT D/IN |
| E9 | USPAT | 2 KLAUBERT, DIETER/IN |
| E10 | USPAT | 22 KLAUBERT, DIETER H/IN |
| E11 | USPAT | 2 KLAUBERT, EARL C/IN |
| E12 | USPAT | 3 KLAUCIC, LUCIANO/IN |

=> s e4

L1 2 "KLATZMANN, DAVID"/IN

=> d l1 cit ab 1-2

1. 5,843,432, Dec. 1, 1998, Retroviral vectors for the treatment of tumors, and cell lines containing them; **David Klatzmann**, et al., 424/93.21; 435/69.1, 320.1, 325 [IMAGE AVAILABLE]

US PAT NO: 5,843,432 [IMAGE AVAILABLE] L1: 1 of 2

ABSTRACT:

The invention relates to recombinant retroviral vectors, derived from Moloney MuLV, carrying a suicide gene susceptible of transforming an inactive substance into a toxic substance for cells going through a division process, said vectors being characterized by the presence in their structure of LTR sequences from variants of MuLV, and having the properties: (a) of not being inactivated during passage through the carcino-embryonic or line germinal cells of mice; (b) the expression of the suicide gene kills only the cells in the course of division.

2. 5,514,542, May 7, 1996, Methods for propagating retrovirus for use in antibody assays; Robert C. Nowinski, et al., 435/5, 7.1, 7.2, 7.9, 7.92, 235.1, 239, 974 [IMAGE AVAILABLE]

US PAT NO: 5,514,542 [IMAGE AVAILABLE] L1: 2 of 2

ABSTRACT:

Cell lines which lack human class II histocompatibility antigens are disclosed. The cell lines may be utilized within a method for propagating microorganisms, such as viruses, for determining the presence and/or amount of antibody to a microorganism in a biological fluid, and within a method for producing antibodies to a selected microorganism.

=> e coen, jacques/in

| E# | FILE | FREQUENCY TERM |
|-----|-------|-----------------------------------|
| E1 | USPAT | 1 COEN, ERNESTO/IN |
| E2 | USPAT | 2 COEN, GUNTHER/IN |
| E3 | USPAT | 0 -> COEN, JACQUES/IN |
| E4 | USPAT | 2 COEN, MANUS/IN |
| E5 | USPAT | 1 COEN, ROBERT/IN |
| E6 | USPAT | 2 COEN, THOMAS P/IN |
| E7 | USPAT | 1 COEN, THOMAS T/IN |
| E8 | USPAT | 1 COENAN, MICHEL J W/IN |
| E9 | USPAT | 2 COENDERS, JOHANNES W/IN |
| E10 | USPAT | 3 COENDERS, JOHANNES WILHELMUS/IN |
| E11 | USPAT | 2 COENDERS, WILLI/IN |
| E12 | USPAT | 1 COENDOZO, JEAN PIERRE/IN |

=> e cohen, jacques/in

| E# | FILE | FREQUENCY TERM |
|-----|-------|---------------------------|
| E1 | USPAT | 2 COHEN, JACOB/IN |
| E2 | USPAT | 5 COHEN, JACOB I/IN |
| E3 | USPAT | 9 -> COHEN, JACQUES/IN |
| E4 | USPAT | 6 COHEN, JAMES/IN |
| E5 | USPAT | 2 COHEN, JAMES A/IN |
| E6 | USPAT | 2 COHEN, JAMES D/IN |
| E7 | USPAT | 2 COHEN, JASON M/IN |
| E8 | USPAT | 1 COHEN, JAY B/IN |
| E9 | USPAT | 1 COHEN, JEAN PIERRE D/IN |
| E10 | USPAT | 1 COHEN, JEANNIE/IN |
| E11 | USPAT | 1 COHEN, JEFFERY M/IN |
| E12 | USPAT | 5 COHEN, JEFFREY/IN |

=> s e3

L2 9 "COHEN, JACQUES"/IN

=> d l2 cit ab 1-9

1. 5,415,155, May 16, 1995, Modular element with multiple conduits; **Jacques Cohen**, et al., 126/663; 138/111, 115, 155 [IMAGE AVAILABLE]

US PAT NO: 5,415,155 [IMAGE AVAILABLE] L2: 1 of 9

ABSTRACT:

This modular element has several conduits disposed side by side, each pair of adjacent conduits being interconnected to form a rigid or flexible unit, each conduit has a male end and an opposite female end, the latter for joining with the male end of an aligned conduit of an adjacent modular element. The several conduits of a first modular element can therefore be simultaneously extended by the several conduits of a second modular element by simultaneously joining the female and male ends of the elements. These elements can be in the form of panels to be joined together to form, for instance, a solar panel or a floor covering with a circulating heat transfer fluid through the conduits. The conduits may also serve as protected passages for underground electrical wires. The conduits may be provided with sprinkler holes to water plants. The panels preferably have interlocking means on their sides which are parallel to the conduits for interlocking adjacent panels and these sides may be provided with fastening zones to fasten the panels to an underlying surface. The panels can be fitted with a transparent cover enclosing an air chamber allowing sun rays therethrough but preventing heat escape when used as solar panels.

2. 5,144,530, Sep. 1, 1992, Power distributor device for electric installations; **Jacques Cohen**, et al., 361/675; 174/99B; 361/638, 649, 439/114, 213, 714, 949 [IMAGE AVAILABLE]

US PAT NO: 5,144,530 [IMAGE AVAILABLE] L2: 2 of 9

ABSTRACT:

A power distributor device is disclosed for electric installations, comprising, for housing a set of power bars, an insulating case formed preferably of several interlockable modules. A member, for example an end-piece in the form of a lyre is associated with a zone for fixing the case on a support allowing expansion between the case and the support. An upstream connection box may be assembled to the case and comprise a zone for fixing to the support.

3. 4,855,698, Aug. 8, 1989, Protective switching apparatus with remotely controlled opening and closing of the contacts; **Jacques Cohen**, et al., 335/14, 20 [IMAGE AVAILABLE]

US PAT NO: 4,855,698 [IMAGE AVAILABLE] L2: 3 of 9

ABSTRACT:

A protective switching apparatus with remote controlled opening and closing is provided including a tripping mechanism connected to an assembly comprising at least two fixed contacts and two mobile contacts and to a magnetic and/or thermal trip; a resetting member and an electromagnet having a movable element and to a member for driving a least one pseudo-fixed or mobile contact. The mobile contacts are carried by a bridge having a plane of symmetry X--X and the tripping mechanism extends in the vicinity of the plane of symmetry X--X. The electromagnet and the trip are housed in the case on each side of the tripping mechanism in a direction perpendicular to the plane of symmetry.

4. 4,650,937, Mar. 17, 1987, Automatic protection switch with visible disconnecting action and manual resetting; Elie Belbel, et al., 200/434, 50.17, 50.21, 61.19, 573 [IMAGE AVAILABLE]

US PAT NO: 4,650,937 [IMAGE AVAILABLE] L2: 4 of 9

ABSTRACT:

An electric switch apparatus for protecting an electric circuit, said apparatus comprising a case, a pivoting drawer connected to the case and adapted to be manually pivoted from a closed position to an open position and reversely, a switch having a fixed and a movable contact, the movable contact being mechanically linked to the drawer for simultaneous

opening

therewith and a breaking member for automatically breaking an electric circuit connected across two terminals of the case, the said breaking member operating in case of an overflow of current in the said circuit, the movable contact being able to be separated from the fixed contact under the action of an actuation member comprising a spring and a magnetizable member, said actuating member cooperating with a coil placed in the circuit and being reset during a manual opening and closing movement of the drawer.

5. D 263,518, Mar. 30, 1982, Sole for footwear; **Jacques Cohen**, D2/954 [IMAGE AVAILABLE]

US PAT NO: D 263,518 [IMAGE AVAILABLE] L2: 5 of 9

6. D 263,348, Mar. 16, 1982, Sole for footwear; **Jacques Cohen**, D2/954 [IMAGE AVAILABLE]

US PAT NO: D 263,348 [IMAGE AVAILABLE] L2: 6 of 9

7. 4,296,396, Oct. 20, 1981, Manual electric switch with thermal release; Raymond A. Ingrain, et al., 337/66, 58, 70 [IMAGE AVAILABLE]

US PAT NO: 4,296,396 [IMAGE AVAILABLE] L2: 7 of 9

ABSTRACT:

In a manual switch with thermal and magnetic release, the fixed pivots of a control member, of a latch, and of a transmission member coupled to the contacts, are disposed at the apices of a right-angled triangle, one side bounding the right angle being parallel to the direction of actuation of the control member and to the movement of the contacts, the other side bounding the right angle being placed in the vicinity of the control member.

8. 4,223,456, Sep. 23, 1980, Shoe sole assembly; **Jacques Cohen**, 36/29, 3B, 32R, 59R [IMAGE AVAILABLE]

US PAT NO: 4,223,456 [IMAGE AVAILABLE] L2: 8 of 9

ABSTRACT:

A shoe sole assembly of a resilient material body portion provided with absorbers energy formed as part of the body portion. The energy absorbers are defined by vertically disposed, spaced apart cell members extending from an upper surface to beyond a lower surface of the body portion to provide a bounded space. Each cell member is formed of an hollow compartment extending in part for the thickness of the body portion with its length depending upon the sole profile, the first end of the respective compartments at the upper surface of the sole body portion is initially open ended; whereas a hollow protuberance structure is at the lower surface of the body portion to enclose each cylindrical compartment at a second end. The protuberances extend beyond the lower surface to form contact areas with the ground surface when the sole assembly is used as part of a shoe. The compartments are separated from one another by adjacent lands which at the upper sole surface provide define respective substrate areas for the disposition of an inner sole thereon, so to seal each cell member with a volume of air trapped in the bounded space of the compartment and associated hollow protuberance structure.

9. 3,839,691, Oct. 1, 1974, SETTING AND TRIGGERING DEVICE FOR THERMAL RELAY; **Jacques Cohen**, et al., 337/132, 66, 72 [IMAGE AVAILABLE]

US PAT NO: 3,839,691 [IMAGE AVAILABLE] L2: 9 of 9

ABSTRACT:

A thermal relay designed to control the power supply circuit of a contactor, said thermal relay comprising movable contacts cooperating with stationary contacts, a triggering slide released by thermoelements for displacing the movable contacts to open the circuit in case of excessive current flow and a hand control, controlling the slide and the movable contacts for opening or closing the circuit. The slide cannot be reset in proper position for closing the circuits unless the thermoelements are cold.

=> s c4bp

L3 44 C4BP

=> s c4bp?

L4 44 C4BP?

=> s 14 and (cd4 or cd8 or cd16 or cd35 or cr1)

2956 CD4
1390 CD8
237 CD16
28 CD35
3679 CR1

L5 22 L4 AND (CD4 OR CD8 OR CD16 OR CD35 OR CR1)

=> s 15 and scfv?

112 SCFV?
L6 0 L5 AND SCFV?

=> s 15 and erythrocyte?

6907 ERYTHROCYTE?
L7 14 L5 AND ERYTHROCYTE?

=> s 17 and (alpha or beta)

270378 ALPHA
181872 BETA
L8 14 L7 AND (ALPHA OR BETA)

=> d 18 cit ab 1-14

1. 5,869,615, Feb. 9, 1999, Modified complement proteases; Dennis E. Hourcade, et al., 530/380; 435/69.1; 530/350 [IMAGE AVAILABLE]

US PAT NO: 5,869,615 [IMAGE AVAILABLE] L8: 1 of 14

ABSTRACT:

Variant complement proteins that are modified in their complement-mediated activity are provided, along with methods for their preparation, and their potential uses. The modifications comprise amino acid substitutions in regions of the complement proteins that contain certain motifs also present in homologous proteins. The amino acid substitutions and their effect on the complement activity of the modified protein are also provided.

2. 5,863,542, Jan. 26, 1999, Recombinant attenuated ALVAC canarypox virus containing heterologous HIV or SIV inserts; Enzo Paoletti, et al., 424/199.1, 188.1, 208.1, 232.1; 435/236 [IMAGE AVAILABLE]

US PAT NO: 5,863,542 [IMAGE AVAILABLE] L8: 2 of 14

ABSTRACT:

Attenuated recombinant viruses containing DNA encoding an immunodeficiency virus and/or CTL antigen, as well as methods and compositions employing the viruses, expression products therefrom, and antibodies generated from the viruses or expression products, are disclosed and claimed. The recombinant viruses can be NYVAC or ALVAC recombinant viruses. The DNA can code for at least one of: HIV1gag(+pro)(IIIB), gp120(MN)(+transmembrane), nef(BRU)CTL, pol(IIIB)CTL, ELDKWA or LDKW epitopes, preferably HIV1gag(+pro)(IIIB), gp120(MN)(+transmembrane), two (2) nef(BRU)CTL and three (3) pol(IIIB)CTL epitopes; or two ELDKWA in gp120 V3 or another region or in gp160. The two (2) nef(BRU)CTL and three (3) pol(IIIB)CTL epitopes are preferably CTL1, CTL2, pol1, pol2 and pol3. The recombinant viruses and gene products therefrom and antibodies generated by the viruses and gene products have several preventive, therapeutic and diagnostic uses. DNA from the recombinant viruses are useful as probes or, for generating PCR primers or for immunization. Also disclosed and claimed are HIV immunogens and modified gp160 and gp120.

3. 5,856,300, Jan. 5, 1999, Compositions comprising complement related proteins and carbohydrates, and methods for producing and using said compositions; Charles W. Rittershaus, et al., 514/12; 424/192.1, 193.1; 435/69.1, 69.6, 85; 436/501, 518; 514/8, 21; 530/395 [IMAGE AVAILABLE]

US PAT NO: 5,856,300 [IMAGE AVAILABLE] L8: 3 of 14

ABSTRACT:

The present invention provides compositions comprising at least one complement moiety and at least one carbohydrate moiety, and

methods of producing such compositions. In particular, the compositions of the invention comprise complement proteins related to the complement receptor type I, and further comprise ligands for intracellular molecules, such as selectins. In a preferred embodiment, the compositions comprise a complement-related protein in combination with the Louis X antigen or the sialyl Lewis X antigen. The compositions of the invention have use in the diagnosis or therapy of disorders involving complement activity and inflammation. Pharmaceutical compositions are also provided for treating or reducing inflammation mediated by inappropriate complement activity and intercellular adhesion.

4. 5,856,297, Jan. 5, 1999, Human C3b/C4b receptor (**CR1**); Douglas T. Fearon, et al., 514/2; 435/69.1; 530/350; 536/23.4 [IMAGE AVAILABLE]

US PAT NO: 5,856,297 [IMAGE AVAILABLE] L8: 4 of 14

ABSTRACT:

Human complement receptor type 1 (**CR1**). Nucleic acid molecules encoding full-length **CR1** protein and fragments thereof having complement regulatory activity are described, as well as recombinant **CR1** protein and polypeptides, vectors for their expression, and cell lines expressing or bearing DNA molecules encoding such proteins and polypeptides, including a soluble **CR1** polypeptide consisting of the extracellular 30 short consensus repeat domains of the mature **CR1** protein. The nucleic acids and polypeptides described are useful in diagnosis and treatment of disorders involving complement activity and inflammation. Compositions useful in therapeutic applications are also disclosed.

5. 5,851,528, Dec. 22, 1998, Methods of inhibiting complement activation; Jone-Long Ko, et al., 424/185.1, 192.1; 514/12; 530/350, 380 [IMAGE AVAILABLE]

US PAT NO: 5,851,528 [IMAGE AVAILABLE] L8: 5 of 14

ABSTRACT:

The present invention relates to novel chimeric proteins comprising a first polypeptide which inhibits complement activation, linked to a second polypeptide which inhibits complement activation, nucleic acids encoding novel chimeric proteins and methods of reducing inflammation with the administration of the chimeric proteins of the invention.

6. 5,840,858, Nov. 24, 1998, Protein purification using immobilized metal affinity chromatography for complement receptor proteins; Thomas Michael Smith, et al., 530/413, 380, 395 [IMAGE AVAILABLE]

US PAT NO: 5,840,858 [IMAGE AVAILABLE] L8: 6 of 14

ABSTRACT:

This invention relates to the application of immobilized metal affinity chromatography to the purification of complement receptor proteins.

7. 5,833,975, Nov. 10, 1998, Canarypox virus expressing cytokine and/or tumor-associated antigen DNA sequence; Enzo Paoletti, et al., 424/93.2; 435/69.3, 69.51, 69.52, 320.1, 456 [IMAGE AVAILABLE]

US PAT NO: 5,833,975 [IMAGE AVAILABLE] L8: 7 of 14

ABSTRACT:

Attenuated vaccinia or canarypox recombinant viruses containing DNA coding for a cytokine and/or a tumor associated antigen, as well as methods and compositions employing the viruses, are disclosed and claimed. The recombinant viruses can be NYVAC or ALVAC recombinant viruses. The DNA can code for at least one of: human tumor necrosis factor, nuclear phosphoprotein p53, wildtype or mutant; human melanoma-associated antigen; IL-2; IFN gamma; IL-4; GMCSF; IL-12; B7; erb-B-2 and carcinoembryonic antigen. The recombinant viruses and gene products therefrom are useful for cancer therapy.

8. 5,679,546, Oct. 21, 1997, Chimeric proteins which block complement activation; Jone-Long Ko, et al., 435/69.2, 69.7, 252.3, 320.1; 530/350, 412; 536/23.4 [IMAGE AVAILABLE]

US PAT NO: 5,679,546 [IMAGE AVAILABLE]

L8: 8 of 1

ABSTRACT:

The present invention relates to novel chimeric proteins comprising a first polypeptide which inhibits complement activation, linked to a second polypeptide which inhibits complement activation, nucleic acids encoding novel chimeric proteins and methods of reducing inflammation with the administration of the chimeric proteins of the invention.

9. 5,514,787, May 7, 1996, DNA sequences encoding human membrane cofactor protein (MCP); John P. Atkinson, 536/23.1; 435/6, 69.1, 810; 536/24.1, 24.3, 24.31, 24.32, 24.33 [IMAGE AVAILABLE]

US PAT NO: 5,514,787 [IMAGE AVAILABLE]

L8: 9 of 1

ABSTRACT:

Human membrane cofactor protein, a protein involved in regulation of complement activity, has been purified to homogeneity. The gene encoding this protein has been retrieved and permits deduction of the entire amino acid sequence and the recombinant production of this material. Pharmaceutical compositions in which MCP is the active ingredient for use in treating autoimmune diseases are also disclosed.

10. 5,472,939, Dec. 5, 1995, Method of treating complement mediated disorders; Douglas T. Fearon, et al., 514/8, 2, 12, 885, 886 [IMAGE AVAILABLE]

US PAT NO: 5,472,939 [IMAGE AVAILABLE]

L8: 10 of 14

ABSTRACT:

The present invention relates to the C3b/C4b receptor (**CR1**) gene and its encoded protein. The invention also relates to **CR1** nucleic acid sequences and fragments thereof comprising 70 nucleotides and their encoded peptides or proteins comprising 24 amino acids. The invention further provides for the expression of the **CR1** protein and fragments thereof. The genes and proteins of the invention have uses in diagnosis and therapy of disorders involving complement activity, and various immune system or inflammatory disorders. In specific embodiments of the present invention detailed in the examples sections infra, the cloning, nucleotide sequence, and deduced amino acid sequence of a full-length **CR1** cDNA and fragments thereof are described. The expression of the **CR1** protein and fragments thereof is also described. Also described is the expression of a secreted **CR1** molecule lacking a transmembrane region. The secreted **CR1** molecule is shown to be useful in reducing damage caused by inflammation and in reducing myocardial infarct size and preventing reperfusion injury.

11. 5,256,642, Oct. 26, 1993, Compositions of soluble complement receptor 1 (**CR1**) and a thrombolytic agent, and the methods of use thereof; Douglas T. Fearon, et al., 514/8; 424/94.63, 94.64; 435/215, 216; 514/2; 530/350 [IMAGE AVAILABLE]

US PAT NO: 5,256,642 [IMAGE AVAILABLE]

L8: 11 of 14

ABSTRACT:

The present invention relates to compositions comprising soluble complement receptor 1 (**CR1**) and a thrombolytic agent. In a specific embodiment, the thrombolytic agent is anisoylated human plasminogen-streptokinase activator complex (ASPAC). The invention further relates to methods for treating thrombotic conditions in humans and animals by administering a composition comprising soluble **CR1** and a thrombolytic agent. In particular, the compositions and methods are useful both for reducing reperfusion injury and ameliorating the other effects of myocardial infarction.

12. 5,252,216, Oct. 12, 1993, Protein purification; Gail Folena-Wasserman, et al., 210/635, 656; 530/380, 413, 416, 417, 420 [IMAGE AVAILABLE]

US PAT NO: 5,252,216 [IMAGE AVAILABLE]

L8: 12 of 14

ABSTRACT:
This invention relates to the application of combination chromatography to the purification of complement receptor proteins.

13. 5,212,071, May 18, 1993, Nucleic acids encoding a human C3b/C4b receptor (**CR1**); Douglas T. Fearon, et al., 435/69.1, 252.3, 320.1; 530/350 [IMAGE AVAILABLE]

US PAT NO: 5,212,071 [IMAGE AVAILABLE] L8: 13 of 14

14. 4,672,044, Jun. 9, 1987, Murine monoclonal antibody combining site to human C3b receptor (**CR1**); Robert D. Schreiber, 436/501; 435/4, 7.21, 7.24, 7.25, 70.21, 334, 810, 968, 975; 436/504, 506, 507, 512, 518, 536, 540, 548, 815, 821 [IMAGE AVAILABLE]

US PAT NO: 4,672,044 [IMAGE AVAILABLE] L8: 14 of 14

ABSTRACT:
A murine monoclonal antibody combining site produced by a hybridoma formed by fusion of cells from a myeloma cell line and lymphocytes that produce antibodies that react (1) with isolated human C3b receptor and (2) with C3b receptor-bearing cells from a mammal immunized with human C3b receptor is disclosed.

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(FILE 'USPAT ENTERED AT 16:05:08 ON 25 APR 1999)
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L1 2 S E4
E COEN, JACQUES/IN
E COHEN, JACQUES/IN
L2 9 S E3
L3 44 S C4BP
L4 44 S C4BP?
L5 22 S L4 AND (CD4 OR CD8 OR CD16 OR CD35 OR CR1)
L6 0 S LS AND SCFV?
L7 14 S LS AND ERYTHROCYTE?
L8 14 S L7 AND (ALPHA OR BETA)

=> d l4 cit 1-44

1. 5,869,615, Feb. 9, 1999, Modified complement proteases; Dennis E. Hourcade, et al., 530/380; 435/69.1; 530/350 [IMAGE AVAILABLE]

2. 5,863,542, Jan. 26, 1999, Recombinant attenuated ALVAC canarypox virus containing heterologous HIV or SIV inserts; Enzo Paoletti, et al., 424/199.1, 188.1, 208.1, 232.1; 435/236 [IMAGE AVAILABLE]

3. 5,858,373, Jan. 12, 1999, Recombinant poxvirus-feline infectious peritonitis virus, compositions thereof and methods for making and using them; Enzo Paoletti, et al., 424/199.1, 186.1, 204.1, 205.1, 221.1, 235.1; 435/69.3, 236, 237; 536/23.71 [IMAGE AVAILABLE]

4. 5,856,300, Jan. 5, 1999, Compositions comprising complement related proteins and carbohydrates, and methods for producing and using said compositions; Charles W. Rittershaus, et al., 514/12; 424/192.1, 193.1; 435/69.1, 69.6, 85; 436/501, 518; 514/8, 21; 530/395 [IMAGE AVAILABLE]

5. 5,856,297, Jan. 5, 1999, Human C3b/C4b receptor (CR1); Douglas T. Fearon, et al., 514/2; 435/69.1; 530/350; 536/23.4 [IMAGE AVAILABLE]

6. 5,851,528, Dec. 22, 1998, Methods of inhibiting complement activation; Jone-Long Ko, et al., 424/185.1, 192.1; 514/12; 530/350, 380 [IMAGE AVAILABLE]

7. 5,849,585, Dec. 15, 1998, Isolating and culturing Schwann cells; Jennie P. Mather, et al., 435/368, 325, 363, 366, 384, 387, 389 [IMAGE AVAILABLE]

8. 5,843,456, Dec. 1, 1998, Alvac poxvirus-rabies compositions and combination compositions and uses; Enzo Paoletti, et al., 424/199.1, 201.1, 202.1, 204.1, 205.1, 218.1, 224.1; 435/69.3, 235.1, 252.3, 320.1; 514/2; 530/350, 826 [IMAGE AVAILABLE]

9. 5,840,858, Nov. 24, 1998, Protein purification using immobilized metal affinity chromatography for complement receptor proteins; Thomas

Michael Smith, et al., 530/413, 380, 395 [IMAGE AVAILABLE]

10. 5,833,975, Nov. 10, 1998, Canarypox virus expressing cytokine and/or tumor-associated antigen DNA sequence; Enzo Paoletti, et al., 424/93.2; 435/69.3, 69.5, 69.51, 69.52, 320.1, 456 [IMAGE AVAILABLE]

11. 5,830,448, Nov. 3, 1998, Compositions and methods for the treatment of tumors; Gordon A. Vehar, 424/85.2, 85.1, 85.5; 514/2; 530/351, 381 [IMAGE AVAILABLE]

12. 5,767,241, Jun. 16, 1998, Soluble form of GMP-140; Rodger P. McEver, 530/350; 435/69.1, 252.3, 254.11, 325; 530/395; 536/23.5 [IMAGE AVAILABLE]

13. 5,766,599, Jun. 16, 1998, Trova fowl pox virus recombinants comprising heterologous inserts; Enzo Paoletti, et al., 424/199.1, 232.1; 435/69.1, 69.3, 235.1, 320.1 [IMAGE AVAILABLE]

14. 5,762,938, Jun. 9, 1998, Modified recombinant vaccinia virus and expression vectors thereof; Enzo Paoletti, et al., 424/199.1, 204.1, 205.1, 232.1; 435/320.1; 536/23.72 [IMAGE AVAILABLE]

15. 5,762,921, Jun. 9, 1998, Composition and methods for the treatment of tumors; Gordon A. Vehar, 424/85.1, 85.2, 85.5, 158.1, 198.1; 514/12; 530/350, 351, 381 [IMAGE AVAILABLE]

16. 5,756,103, May 26, 1998, Alvac canarypox virus recombinants comprising heterologous inserts; Enzo Paoletti, et al., 424/199.1, 204.1, 206.1, 207.1, 208.1, 214.1, 232.1; 435/69.3, 173.3, 235.1, 252.3, 320.1; 530/350, 826 [IMAGE AVAILABLE]

17. 5,756,102, May 26, 1998, Poxvirus-canine distemper virus (CDV) recombinants and compositions and methods employing the recombinants; Enzo Paoletti, et al., 424/199.1, 213.1, 232.1; 435/69.3, 235.1, 320.1 [IMAGE AVAILABLE]

18. 5,721,139, Feb. 24, 1998, Isolating and culturing schwann cells; Jennie P. Mather, et al., 435/383, 325, 363, 366, 368, 384, 387 [IMAGE AVAILABLE]

19. 5,719,127, Feb. 17, 1998, Modified complement system regulators; John P. Atkinson, et al., 514/12; 530/350 [IMAGE AVAILABLE]

20. 5,714,385, Feb. 3, 1998, Media for culturing schwann cells; Jennie P. Mather, et al., 435/406, 404, 405 [IMAGE AVAILABLE]

21. 5,688,920, Nov. 18, 1997, Nucleotide and amino acid sequences for canine herpesvirus GB, GC and GD and uses therefor; Enzo Paoletti, et al., 530/395; 424/184.1, 199.1, 229.1, 232.1; 435/69.1, 69.3, 235.1, 236, 237, 320.1; 530/350, 403 [IMAGE AVAILABLE]

22. 5,679,546, Oct. 21, 1997, Chimeric proteins which block complement activation; Jone-Long Ko, et al., 435/9.2, 69.7, 252.3, 320.1; 530/350, 412; 536/23.4 [IMAGE AVAILABLE]

23. 5,663,142, Sep. 2, 1997, Protein S deletion variants deficient in **C4BP** binding activity, but having APC cofactor activity, compositions and therapeutic methods; Bonno Namnen Bouma, et al., 514/12; 530/380 [IMAGE AVAILABLE]

24. 5,656,484, Aug. 12, 1997, Protein S deletion variants deficient in **C4BP** binding activity but having APC cofactor activity compositions and therapeutic methods; Bonno Namnen Bouma, et al., 435/252.3, 320.1; 536/23.5 [IMAGE AVAILABLE]

25. 5,545,619, Aug. 13, 1996, Modified complement system regulators; John P. Atkinson, et al., 514/12; 530/350 [IMAGE AVAILABLE]

26. 5,529,780, Jun. 25, 1996, Nucleotide and amino acid sequences of canine herpesvirus gB and gC; Enzo Paoletti, et al., 424/199.1, 184.1, 229.1, 232.1; 435/69.1, 69.3, 235.1, 236, 237, 320.1, 456; 536/23.72, 24.1 [IMAGE AVAILABLE]

27. 5,525,708, Jun. 11, 1996, Covalent dimer of kit ligand; Karl H. Nocka, et al., 530/409, 351, 399, 417 [IMAGE AVAILABLE]

28. 5,514,787, May 7, 1996, DNA sequences encoding human membrane cofactor protein (MCP); John P. Atkinson, 536/23.1; 435/6, 69.1, 810; 536/24.1, 24.3, 24.31, 24.32, 24.33 [IMAGE AVAILABLE]

29. 5,494,807, Feb. 27, 1996, NYVAC vaccinia virus recombinants comprising heterologous inserts; Enzo Paoletti, et al., 435/69.3; 424/199.1, 204.1, 205.1, 218.1, 224.1, 227.1, 229.1, 230.1, 231.1, 232.1; 435/235.1, 320.1; 514/2; 530/350, 826 [IMAGE AVAILABLE]

30. 5,472,939, Dec. 5, 1995, Method of treating complement mediated disorders; Douglas T. Fearon, et al., 514/8, 2, 12, 885, 886 [IMAGE AVAILABLE]

31. 5,405,946, Apr. 11, 1995, Recombinant protein S variants deficient in **C4BP** binding activity, compositions and therapeutic methods; John H. Griffin, et al., 530/380; 435/69.6; 530/830 [IMAGE AVAILABLE]

32. 5,378,464, Jan. 3, 1995, Modulation of inflammatory responses by administration of GMP-140 or antibody to GMP-140; Rodger P. McEver, 514/13; 514/8 [IMAGE AVAILABLE]

33. 5,366,861, Nov. 22, 1994, Immunoassay and reagent kit used therefor; Kenji Hosoda, et al., 435/7.1, 7.92, 7.93, 7.94, 7.95, 15, 975; 436/536 [IMAGE AVAILABLE]

34. 5,364,773, Nov. 15, 1994, Genetically engineered vaccine strain; Enzo Paoletti, et al., 435/69.1; 424/205.1, 232.1; 435/69.3, 235.1, 236, 320.1, 456; 530/300, 350 [IMAGE AVAILABLE]

35. 5,321,123, Jun. 14, 1994, Protein S polypeptides and anti-peptide antibodies that inhibit protein S binding to C4B binding protein, diagnostic systems and therapeutic methods; John H. Griffin, et al., 530/300; 435/7.9; 436/501; 530/324, 325, 327, 328, 329, 830 [IMAGE AVAILABLE]

36. 5,256,642, Oct. 26, 1993, Compositions of soluble complement receptor 1 (CR1) and a thrombolytic agent, and the methods of use thereof; Douglas T. Fearon, et al., 514/8; 424/94.63, 94.64; 435/215, 216; 514/2; 530/350 [IMAGE AVAILABLE]

37. 5,252,216, Oct. 12, 1993, Protein purification; Gail Folena-Wasserman, et al., 210/635, 656; 530/380, 413, 416, 417, 420 [IMAGE AVAILABLE]

38. 5,221,628, Jun. 22, 1993, Binding of aggregated immunoglobulin or immune complexes by serum amyloid P component; Byron E. Anderson, et al., 436/507; 435/7.1, 7.8, 975; 436/501, 509, 518, 536, 538, 808 [IMAGE AVAILABLE]

39. 5,221,616, Jun. 22, 1993, Prevention of spontaneous complement activation in mammalian biological fluids; William P. Kolb, et al., 435/18; 436/69 [IMAGE AVAILABLE]

40. 5,212,071, May 18, 1993, Nucleic acids encoding a human C3b/C4b receptor (CR1); Douglas T. Fearon, et al., 435/69.1, 252.3, 320.1; 530/350 [IMAGE AVAILABLE]

41. 5,198,534, Mar. 30, 1993, Process for preparation of activated protein C by immobilized aprotinin chromatography; Marion Steinbuch, et al., 530/381, 380, 413 [IMAGE AVAILABLE]

42. 5,198,424, Mar. 30, 1993, Functionally active selectin-derived peptides; Rodger P. McEver, 514/13; 424/1.37, 1.69, 427/2.24, 2.25; 514/12, 14, 15, 16; 530/324, 325, 326, 327; 623/11 [IMAGE AVAILABLE]

43. 5,187,067, Feb. 16, 1993, Immunological determination of free human protein S and **C4bp**-protein S complex; Yukiya Koike, et al., 435/7.9, 7.1, 337; 436/821, 824; 530/387.1, 388.25, 412, 413 [IMAGE AVAILABLE]

44. 4,672,044, Jun. 9, 1987, Murine monoclonal antibody combining site to human C3b receptor (CR1); Robert D. Schreiber, 436/501; 435/4, 7.21, 7.24, 7.25, 70.21, 334, 810, 968, 975; 436/504, 506, 507, 512, 518, 536, 540, 548, 815, 821 [IMAGE AVAILABLE]

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E KLATZMAN, DAVID/IN

L1 2 S E4
E COEN, JACQUES/IN
E COHEN, JACQUES/IN
L2 9 S E3

L3 44 S C4BP

L4 44 S C4BP?

L5 22 S L4 AND (CD4 OR CD8 OR CD16 OR CD35 OR CR1)

L6 0 S LS AND SCFV?

L7 14 S LS AND ERYTHROCYTE?

L8 14 S L7 AND (ALPHA OR BETA)

=> s L3 and (coagulation or complement)

20903 COAGULATION
42600 COMPLEMENT
L9 43 L3 AND (COAGULATION OR COMPLEMENT)

=> s l9 and (s protein or scr*)

1635834 S
70853 PROTEIN
528 S PROTEIN
(S(W)PROTEIN)

TERM 'SCR*' EXCEEDED TRUNCATION LIMITS - SEARCH
ENDED

=> s l9 and (s protein or scr or scrs)

1635834 S
70853 PROTEIN
528 S PROTEIN
(S(W)PROTEIN)
12768 SCR
2046 SCRS

L10 23 L9 AND (S PROTEIN OR SCR OR SCRS)

=> d l10 cit ab 1-23

1. 5,869,615, Feb. 9, 1999, Modified **complement** proteases; Dennis E. Hourcade, et al., 530/380; 435/69.1; 530/350 [IMAGE AVAILABLE]

US PAT NO: 5,869,615 [IMAGE AVAILABLE] L10: 1 of 23

ABSTRACT:
Variant **complement** proteins that are modified in their **complement**-mediated activity are provided, along with methods for their preparation, and their potential uses. The modifications comprise amino acid substitutions in regions of the **complement** proteins that contain certain motifs also present in homologous proteins. The amino acid substitutions and their effect on the **complement** activity of the modified protein are also provided.

2. 5,856,300, Jan. 5, 1999, Compositions comprising **complement**-related proteins and carbohydrates, and methods for producing and using said compositions; Charles W. Rittershaus, et al., 514/12; 424/192.1, 193.1; 435/69.1, 69.6, 85; 436/501, 518; 514/8, 21; 530/395 [IMAGE AVAILABLE]

US PAT NO: 5,856,300 [IMAGE AVAILABLE] L10: 2 of 23

ABSTRACT:

The present invention provides compositions comprising at least one **complement** moiety and at least one carbohydrate moiety, and methods of producing such compositions. In particular, the compositions of the invention comprise **complement** proteins related to the **complement** receptor type I, and further comprise ligands for intracellular molecules, such as selectins. In a preferred embodiment, the compositions comprise a **complement**-related protein in combination with the Louis X antigen or the sialyl Lewis X antigen. The compositions of the invention have use in the diagnosis or therapy of disorders involving **complement** activity and inflammation. Pharmaceutical compositions are also provided for treating or reducing inflammation mediated by inappropriate **complement** activity and intercellular adhesion.

3. 5,856,297, Jan. 5, 1999, Human C3b/C4b receptor (CR1); Douglas T. Fearon, et al., 514/2; 435/69.1; 530/350; 536/23.4 [IMAGE AVAILABLE]

US PAT NO: 5,856,297 [IMAGE AVAILABLE] L10: 3 of 23

ABSTRACT:
Human **complement** receptor type I (CR1). Nucleic acid molecules encoding full-length CR1 protein and fragments thereof having **complement** regulatory activity are described, as well as recombinant CR1 protein and polypeptides, vectors for their expression, and cell lines expressing or bearing DNA molecules encoding such proteins and polypeptides, including a soluble CR1 polypeptide consisting of the extracellular 30 short consensus repeat domains of the mature CR1 protein. The nucleic acids and polypeptides described are useful in diagnosis and treatment of disorders involving **complement**.

activity and inflammation. Compositions useful in therapeutic applications are also disclosed.

4. 5,851,528, Dec. 22, 1998, Methods of inhibiting **complement** activation; Jone-Long Ko, et al., 424/185.1, 192.1; 514/12; 530/350, 380

[IMAGE AVAILABLE]

US PAT NO: 5,851,528 [IMAGE AVAILABLE] L10: 4 of 23

ABSTRACT:

The present invention relates to novel chimeric proteins comprising a first polypeptide which inhibits **complement** activation, linked to a second polypeptide which inhibits **complement** activation, nucleic acids encoding novel chimeric proteins and methods of reducing inflammation with the administration of the chimeric proteins of the invention.

5. 5,840,858, Nov. 24, 1998, Protein purification using immobilized metal affinity chromatography for **complement** receptor proteins; Thomas Michael Smith, et al., 530/413, 380, 395 [IMAGE AVAILABLE]

US PAT NO: 5,840,858 [IMAGE AVAILABLE] L10: 5 of 23

ABSTRACT:

This invention relates to the application of immobilized metal affinity chromatography to the purification of **complement** receptor proteins.

6. 5,830,448, Nov. 3, 1998, Compositions and methods for the treatment of tumors; Gordon A. Vehar, 424/85.2, 85.1, 85.5; 514/2; 530/351, 381 [IMAGE AVAILABLE]

US PAT NO: 5,830,448 [IMAGE AVAILABLE] L10: 6 of 23

ABSTRACT:

The invention concerns a method for inhibiting the growth and/or causing regression of tumors by administering a therapeutically effective dose of a procoagulant and a cytokine, preferably TNF-beta., TNF-alpha. and/or IL-1. In a specific aspect, the invention concerns a method for tumor treatment by the administration of a therapeutically effective amount of a thrombomodulin inhibitor and a cytokine. The invention also concerns thrombomodulin inhibitors and pharmaceutical compositions used in the course of these treatments.

7. 5,767,241, Jun. 16, 1998, Soluble form of GMP-140; Rodger P. McEver, 530/350; 435/69.1, 252.3, 254.11, 325; 530/395; 536/23.5 [IMAGE AVAILABLE]

US PAT NO: 5,767,241 [IMAGE AVAILABLE] L10: 7 of 23

ABSTRACT:

The invention is directed to a purified soluble form of human granule membrane protein 140 (GMP-140) which lacks an amino acid sequence comprising a transmembrane domain and which is effective in inhibiting leukocyte adherence mediated by granule membrane protein 140. Nucleic acid encoding the soluble form of GMP-140 is disclosed.

8. 5,766,599, Jun. 16, 1998, Trova fowl pox virus recombinants comprising heterologous inserts; Enzo Paoletti, et al., 424/199.1, 232.1; 435/69.1, 69.3, 235.1, 320.1 [IMAGE AVAILABLE]

US PAT NO: 5,766,599 [IMAGE AVAILABLE] L10: 8 of 23

ABSTRACT:

What is described is a modified vector, such as a recombinant poxvirus, particularly recombinant vaccinia virus, having enhanced safety. The modified recombinant virus has nonessential virus-encoded genetic functions inactivated therein so that virus has attenuated virulence. In one embodiment, the genetic functions are inactivated by deleting an open reading frame encoding a virulence factor. In another embodiment, the genetic functions are inactivated by insertional inactivation of an open reading frame encoding a virulence factor. What is also described is a vaccine containing the modified recombinant virus having nonessential virus-encoded genetic functions inactivated therein so that the vaccine has an increased level of safety compared to known recombinant viruses.

vaccine containing the modified recombinant virus having nonessential virus-encoded genetic functions inactivated therein so that the vaccine has an increased level of safety compared to known recombinant viruses.

9. 5,762,938, Jun. 9, 1998, Modified recombinant vaccinia virus and expression vectors thereof; Enzo Paoletti, et al., 424/199.1, 204.1, 205.1, 232.1; 435/320.1; 536/23.72 [IMAGE AVAILABLE]

US PAT NO: 5,762,938 [IMAGE AVAILABLE] L10: 9 of 23

ABSTRACT:

What is described is a modified vector, such as a recombinant poxvirus, particularly recombinant vaccinia virus, having enhanced safety. The modified recombinant virus has nonessential virus-encoded genetic functions inactivated therein so that virus has attenuated virulence. In one embodiment, the genetic functions are inactivated by deleting an open reading frame encoding a virulence factor. In another embodiment, the genetic functions are inactivated by insertional inactivation of an open reading frame encoding a virulence factor. What is also described is a vaccine containing the modified recombinant virus having nonessential virus-encoded genetic functions inactivated therein so that the vaccine has an increased level of safety compared to known recombinant viruses.

10. 5,762,921, Jun. 9, 1998, Composition and methods for the treatment of tumors; Gordon A. Vehar, 424/85.1, 85.2, 85.5, 158.1, 198.1; 514/12; 530/350, 351, 381 [IMAGE AVAILABLE]

US PAT NO: 5,762,921 [IMAGE AVAILABLE] L10: 10 of 23

ABSTRACT:

The invention concerns a method for inducing a selective collapse of the vasculature of a solid tumor by administering to a patient a therapeutically effective dose of a combination of a compound preventing the formation of a functional thrombin-thrombomodulin complex and a cytokine selected from the group of TNF-beta. (LT), TNF-alpha., IL-1, and IFN-gamma.. The invention further concerns the composition used in this method.

11. 5,756,103, May 26, 1998, Alvac canarypox virus recombinants comprising heterologous inserts; Enzo Paoletti, et al., 424/199.1, 204.1, 206.1, 207.1, 208.1, 214.1, 232.1; 435/69.3, 173.3, 235.1, 252.3, 320.530/350, 826 [IMAGE AVAILABLE]

US PAT NO: 5,756,103 [IMAGE AVAILABLE] L10: 11 of 23

ABSTRACT:

What is described is a modified vector, such as a recombinant poxvirus, particularly recombinant vaccinia virus, having enhanced safety. The modified recombinant virus has nonessential virus-encoded genetic functions inactivated therein so that virus has attenuated virulence. In one embodiment, the genetic functions are inactivated by deleting an open reading frame encoding a virulence factor. In another embodiment, the genetic functions are inactivated by insertional inactivation of an open reading frame encoding a virulence factor. What is also described is a vaccine containing the modified recombinant virus having nonessential virus-encoded genetic functions inactivated therein so that the vaccine has an increased level of safety compared to known recombinant viruses.

12. 5,719,127, Feb. 17, 1998, Modified **complement** system regulators; John P. Atkinson, et al., 514/12; 530/350 [IMAGE AVAILABLE]

US PAT NO: 5,719,127 [IMAGE AVAILABLE] L10: 12 of 23

ABSTRACT:

Analogs of regulators of **complement** activation (RCA) proteins which have altered specificities and affinities for the targets C3b and/or C4b are described. These analogs are obtained by substituting amino acids which effect the binding of these proteins, identified as amino acids 35, 64-65, 92-94 (C4b) and the sequence S-T-K-P-(P-I-C)-Q (C3b) in the CR1 protein can be transferred to corresponding regions of CR1 or of

additional members of the RCA family. Analogs can also be designed by substituting amino acids which affect the binding of these proteins into homologous regions of noncorresponding **SCRs** of CR1 or other family members.

13. 5,679,546, Oct. 21, 1997, Chimeric proteins which block **complement** activation; Jone-Long Ko, et al., 435/69.2, 69.7, 252.3, 320.1; 530/350, 412; 536/23.4 [IMAGE AVAILABLE]

US PAT NO: 5,679,546 [IMAGE AVAILABLE] L10: 13 of 23

ABSTRACT:
The present invention relates to novel chimeric proteins comprising a first polypeptide which inhibits **complement** activation, linked to a second polypeptide which inhibits **complement** activation, nucleic acids encoding novel chimeric proteins and methods of reducing inflammation with the administration of the chimeric proteins of the invention.

14. 5,545,619, Aug. 13, 1996, Modified **complement** system regulators; John P. Atkinson, et al., 514/12; 530/350 [IMAGE AVAILABLE]

US PAT NO: 5,545,619 [IMAGE AVAILABLE] L10: 14 of 23

ABSTRACT:
Analogs of regulators of **complement** activation (RCA) proteins which have altered specificities and affinities for the targets C3b and/or C4b are described. These analogs are obtained by substituting amino acids which effect the binding of these proteins, identified as amino acids 35, 64-65, 92-94 (C4b) and the sequence S-T-K-P-(P-I-C)-Q (SEQ ID NO:1) (C3b) in the CR1 protein can be transferred to corresponding regions of CR1 or of additional members of the RCA family. Analogs can also be designed by substituting amino acids which affect the binding of these proteins into homologous regions of noncorresponding **SCRs** of CR1 or other family members.

15. 5,494,807, Feb. 27, 1996, NYVAC vaccinia virus recombinants comprising heterologous inserts; Enzo Paoletti, et al., 435/69.3; 424/199.1, 204.1, 205.1, 218.1, 224.1, 227.1, 229.1, 230.1, 231.1, 232.1, 239.1; 435/235.1, 320.1; 514/2; 530/350, 826 [IMAGE AVAILABLE]

US PAT NO: 5,494,807 [IMAGE AVAILABLE] L10: 15 of 23

ABSTRACT:
What is described is a modified vector, such as a recombinant poxvirus, particularly recombinant vaccinia virus, having enhanced safety. The modified recombinant virus has nonessential virus-encoded genetic functions inactivated therein so that virus has attenuated virulence. In one embodiment, the genetic functions are inactivated by deleting an open reading frame encoding a virulence factor. In another embodiment, the genetic functions are inactivated by insertional inactivation of an open reading frame encoding a virulence factor. What is also described is a vaccine containing the modified recombinant virus having nonessential virus-encoded genetic functions inactivated therein so that the vaccine has an increased level of safety compared to known recombinant virus vaccines.

16. 5,472,939, Dec. 5, 1995, Method of treating **complement** mediated disorders; Douglas T. Fearon, et al., 514/8, 2, 12, 885, 886 [IMAGE AVAILABLE]

US PAT NO: 5,472,939 [IMAGE AVAILABLE] L10: 16 of 23

ABSTRACT:
The present invention relates to the C3b/C4b receptor (CR1) gene and its encoded protein. The invention also relates to CR1 nucleic acid sequences and fragments thereof comprising 70 nucleotides and their encoded peptides or proteins comprising 24 amino acids. The invention further provides for the expression of the CR1 protein and fragments thereof. The genes and proteins of the invention have uses in diagnosis and therapy of disorders involving **complement** activity, and various immune system or

inflammatory disorders. In specific embodiments of the present invention detailed in the examples sections infra, the cloning, nucleotide sequence, and deduced amino acid sequence of a full-length CR1 cDNA and fragments thereof are described. The expression of the CR1 protein and fragments thereof is also described. Also described is the expression of a secreted CR1 molecule lacking a transmembrane region. The secreted CR1 molecule is shown to be useful in reducing damage caused by inflammation and in reducing myocardial infarct size and preventing reperfusion injury.

17. 5,405,946, Apr. 11, 1995, Recombinant protein S variants deficient in **C4BP** binding activity, compositions and therapeutic methods; John H. Griffin, et al., 530/380; 435/69.6; 530/830 [IMAGE AVAILABLE]

US PAT NO: 5,405,946 [IMAGE AVAILABLE] L10: 17 of 23

ABSTRACT:
The present invention describes a variant protein **S** **protein** that is substantially homologous in amino acid residue sequence to wild-type mature human protein S, which has in vitro anticoagulant activity and has a reduced ability to bind C4b binding protein (**C4BP**), compositions containing the variant protein S, and recombinant DNA vectors for expressing the variant protein. Also disclosed are therapeutic methods of using variant protein S for inhibiting thrombosis, inflammation and like conditions ameliorated by protein S.

18. 5,378,464, Jan. 3, 1995, Modulation of inflammatory responses by administration of GMP-140 or antibody to GMP-140; Rodger P. McEver, 424/143.1; 514/8 [IMAGE AVAILABLE]

US PAT NO: 5,378,464 [IMAGE AVAILABLE] L10: 18 of 23

ABSTRACT:
A method using compounds inhibiting binding reactions involving GMP-140 to modulate an inflammatory response. The method is based on the discovery that GMP-140, released from the storage granules of platelets, endothelial cells, and megakaryocytes, and redistributed to the surface of the cells within seconds of activation by mediators such as thrombin, ionophores or histamine, binds to a ligand on neutrophils, and the plasma proteins C3b and protein S. Adhesion of the cells following activation is blocked directly by administration of antibody to GMP-140 or its ligand, or by competitive inhibition by administration of soluble GMP-140, the GMP-140 ligand, or the specific carbohydrate portion of the ligand bound by GMP-140.

19. 5,321,123, Jun. 14, 1994, Protein S polypeptides and anti-peptide antibodies that inhibit protein S binding to C4B binding protein, diagnostic systems and therapeutic methods; John H. Griffin, et al., 530/300; 435/7.93; 436/501; 530/324, 325, 327, 328, 329, 830 [IMAGE AVAILABLE]

US PAT NO: 5,321,123 [IMAGE AVAILABLE] L10: 19 of 23

ABSTRACT:
The invention describes protein S polypeptides and anti-PS antibodies capable of inhibiting the binding of proteins to **C4BP**. The peptides and antibodies are useful in diagnostic methods and systems for purifying or detecting free protein S. In addition, the polypeptides are useful in therapeutic methods as an anti-coagulant.

20. 5,256,642, Oct. 26, 1993, Compositions of soluble **complement** receptor 1 (CR1) and a thrombolytic agent, and the methods of use thereof; Douglas T. Fearon, et al., 514/8, 424/94.63, 94.64; 435/215, 216; 514/2; 530/350 [IMAGE AVAILABLE]

US PAT NO: 5,256,642 [IMAGE AVAILABLE] L10: 20 of 23

ABSTRACT:
The present invention relates to compositions comprising soluble

complement receptor 1 (CR1) and a thrombolytic agent. In a specific embodiment, the thrombolytic agent is anisoylated human plasminogen-streptokinase activator complex (ASPAc). The invention further relates to methods for treating thrombotic conditions in humans and animals by administering a composition comprising soluble CR1 and a thrombolytic agent. In particular, the compositions and methods are useful both for reducing reperfusion injury and ameliorating the other effects of myocardial infarction.

21. 5,252,216, Oct. 12, 1993, Protein purification; Gail Folena-Wasserman, et al., 210/635, 656; 530/380, 413, 416, 417, 420 [IMAGE AVAILABLE]

US PAT NO: 5,252,216 [IMAGE AVAILABLE] L10: 21 o 23

ABSTRACT:
This invention relates to the application of combination chromatography to the purification of **complement** receptor proteins.

22. 5,221,616, Jun. 22, 1993, Prevention of spontaneous **complement** activation in mammalian biological fluids; William P. Kolb, et al., 435/18; 436/69 [IMAGE AVAILABLE]

US PAT NO: 5,221,616 [IMAGE AVAILABLE] L10: 22 o 23

ABSTRACT:
Selected polyhydroxyl compounds, comprising monosaccharides, disaccharides and oligosaccharides, as well as certain of their derivatives, are effective in preventing the spontaneous activation of **complement** in vitro. The effect is enhanced in the presence of an anticoagulant together with a divalent cation chelator. Addition of these compounds makes it possible to store clinical samples at conventional temperatures from -20.degree. to +22.degree. C. for extended periods prior to performing **complement** protein assays. Effective compounds are selected through a screening protocol which comprises the use of immunoassays for **complement** fragments together with an algorithm for computing effectiveness. Polyhydroxyl compounds extend similar protection from activation to **coagulation** proteins.

23. 5,212,071, May 18, 1993, Nucleic acids encoding a human C3b/C4b receptor (CR1); Douglas T. Fearon, et al., 435/69.1, 252.3, 320.1; 530/350 [IMAGE AVAILABLE]

US PAT NO: 5,212,071 [IMAGE AVAILABLE] L10: 23 o 23

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E KLATZMAN, DAVID/IN
L1 2 S E4
E COEN, JACQUES/IN
E COHEN, JACQUES/IN
L2 9 S E3
L3 44 S C4BP
L4 44 S C4BP?
L5 22 S L4 AND (CD4 OR CD8 OR CD16 OR CD35 OR CR1
L6 0 S L5 AND SCFV?
L7 14 S L5 AND ERYTHROCYTE?
L8 14 S L7 AND (ALPHA OR BETA)
L9 43 S L3 AND (COAGULATION OR COMPLEMENT)
L10 23 S L9 AND (S PROTEIN OR SCR OR SCRS)

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| FULL ESTIMATED COST | | 0.15 | 0.15 |

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SEARCH ENDED BY USER

=> s c4bp

L1 983 C4BP

=> s l1 and (cd4 or cd8 or cd16 or cd35 or cr1)

L2 106 L1 AND (CD4 OR CD8 OR CD16 OR CD35 OR CR1)

=> s l2 and (coagulation or complement)

L3 103 L2 AND (COAGULATION OR COMPLEMENT)

=> s l3 and erythrocyte?

L4 18 L3 AND ERYTHROCYTE?

=> s l3 and c terminal

L5 1 L3 AND C TERMINAL

=> s l2 and ratio

L6 0 L2 AND RATIO

=> s l1 and (anti-rh or anti rh)

L7 6 L1 AND (ANTI-RH OR ANTI RH)

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1 FILES SEARCHED...

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L8 4 L3 AND S PROTEIN?

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L1 983 S C4BP

L2 106 S L1 AND (CD4 OR CD8 OR CD16 OR CD35 OR
CR1)

L3 103 S L2 AND (COAGULATION OR COMPLEMENT)

L4 18 S L3 AND ERYTHROCYTE?

L5 1 S L3 AND C TERMINAL

L6 0 S L2 AND RATIO

L7 6 S L1 AND (ANTI-RH OR ANTI RH)

L8 4 S L3 AND S PROTEIN?

=> dup rem l2

PROCESSING COMPLETED FOR L2

L9 46 DUP REM L2 (60 DUPLICATES REMOVED)

=> dup rem l4

PROCESSING COMPLETED FOR L4

L10 8 DUP REM L4 (10 DUPLICATES REMOVED)

=> dup rem l7

PROCESSING COMPLETED FOR L7

L11 2 DUP REM L7 (4 DUPLICATES REMOVED)

=> dup rem l8

PROCESSING COMPLETED FOR L8

L12 4 DUP REM L8 (0 DUPLICATES REMOVED)

=> d i9 ibib abs 1-46

L9 ANSWER 1 OF 46 BIOSIS COPYRIGHT 1999 BIOSIS
ACCESSION NUMBER: 1999:144622 BIOSIS
DOCUMENT NUMBER: PREV199900144622
TITLE: Antibody recognition of complement regulatory
proteins,

factor H, ***CR1*** and ***C4BP*** in
antiphospholipid syndrome patients.

AUTHOR(S): Guerin, J. (1); Sim, R. B.; Feighery, C. (1);
Jackson, J.

(1)

CORPORATE SOURCE: (1) Dep. Immunol., St. James's Hosp.,
Dublin Ireland

SOURCE: Lupus, (1998) Vol. 7, No. SUPPL. 2, pp. S180.
Meeting Info.: 8th International Symposium on
Antiphospholipid Antibodies Sapporo, Japan October

6-9,

1998

ISSN: 0961-2033.
DOCUMENT TYPE: Conference
LANGUAGE: English

L9 ANSWER 2 OF 46 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1997:267203 CAPLUS
DOCUMENT NUMBER: 126:250213
TITLE: Recombinant heteromultimeric C4 binding protein
fusion
proteins and their use for vaccines, immunotherapy
and
diagnosis
INVENTOR(S): Klatzmann, David; Cohen, Jacques
PATENT ASSIGNEE(S): Universite de Reims Champagne
Ardennes, Fr.; Universite Pierre et Marie Curie Paris VI
SOURCE: Fr. Demande, 36 pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. |
|---|------|----------|------------------------|
| FR 2736916 | A1 | 19970124 | FR 95-8901 19950721 |
| FR 2736916 | B1 | 19970919 | |
| WO 9704109 | A1 | 19970206 | WO 96-FR1132 19960718 |
| W: CA, JP, US | | | |
| RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | |
| CA 2227030 | AA | 19970206 | CA 96-2227030 19960718 |
| EP 842282 | A1 | 19980520 | EP 96-926424 19960718 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | |
| PRIORITY APPLN. INFO.: | | | FR 95-8901 19950721 |
| | | | WO 96-FR1132 19960718 |

AB Disclosed are recombinant multimeric proteins comprising at least (a)
fusion protein A contg. C4 binding protein (***C4BP***)
alpha, chain
C-terminal residues 124-549 and a heterologous protein and (b)
fusion
protein B contg. ***C4BP*** .beta. chain C-terminal residues 120-235
and a heterologous protein, the proteins A and B binding to each other
through the C-terminal domains to form the multimeric protein.
Recombinant cells producing the multimeric proteins as well as use of the
heterooligomers or cells for fetal-maternal alloimmunization, for therapy
or prophylaxis of infections, for therapy of autoimmune diseases, for
immunotherapy and for diagnosis are also disclosed. Thus,
anti-Rh(D)
scFv- ***C4BP*** and CD43 fragment- ***C4BP*** fusion proteins were
produced with CHO cells. The heterooligomeric protein formed agglutinated
Rh+ erythrocytes.

L9 ANSWER 3 OF 46 BIOSIS COPYRIGHT 1999 BIOSIS
ACCESSION NUMBER: 1997:369854 BIOSIS
DOCUMENT NUMBER: PREV199799669057
TITLE: The use of RCA YACs to generate transgenic animals
expressing genes of the human regulators of complement activation.
AUTHOR(S): Weiss, E. H.; Sprinks, M. T.; Besenfelder, U.;
Cannich, A.; Mueller, S.; Brem, G.
CORPORATE SOURCE: Inst. Anthropol. Humangenet.,
Ludwig-Maximilians-Univ.
SOURCE: Experimental and Clinical Immunogenetics, (1997)
Vol. 14,
No. 1, pp. 107.
Meeting Info.: 6th European Meeting on Complement in
Human Disease Innsbruck, Austria March 12-15, 1997
ISSN: 0254-9670.
DOCUMENT TYPE: Conference; Abstract
LANGUAGE: English

L9 ANSWER 4 OF 46 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1996:479450 CAPLUS
DOCUMENT NUMBER: 125:107075
TITLE: Transgene construct using locus control region
upstream of gene of interest, improved expression in
transgenic animal, and xenograft implant hyperacute
rejection
INVENTOR(S): Colman, Alan
PATENT ASSIGNEE(S): Ppl Therapeutics (Scotland) Ltd., UK
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXX2D
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. |
|---|------|----------|-----------------------|
| WO 9617946 | A1 | 19960613 | WO 95-GB2839 19951206 |
| W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, LZ, LR, LS, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK | | | |
| RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | |
| AU 9539906 | A1 | 19960626 | AU 95-39906 19951206 |
| PRIORITY APPLN. INFO.: | | | GB 94-24550 19941206 |
| | | | WO 95-GB2839 19951206 |

AB The application identifies a problem in the expression of transgenes in
transgenic animals which renders the use of transgenic material unsuitable
for successful xenograft transplantation. The difficulty identified is the
variated expression of the transgene which renders the xenograft
vulnerable to hyperacute rejection after implantation. The soln.
described is to include a region corresponding to a substantial portion of
the region naturally upstream of the gene of interest. Preferably the
region includes the locus control region (LCR) for the gene of interest,
preferably together with the intervening section which naturally links the
LCR to the gene of interest. The transgene construct described is therefore extremely large and is desirably manipulated and amplified using
YAC technol.

L9 ANSWER 5 OF 46 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1996:607743 CAPLUS
DOCUMENT NUMBER: 125:245269
TITLE: Identification of three physically and functionally distinct binding sites for C3b in human complement factor H by deletion mutagenesis
AUTHOR(S): Sharma, Ajay K.; Pangburn, Michael K.
CORPORATE SOURCE: Department Biochemistry, University Texas Health

Science Center, Tyler, TX, 75710-2003, USA
SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1996), 93(20),
10996-11001
CODEN: PNAS6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Human complement factor H controls spontaneous activation of complement in plasma and appears to play a role in distinguishing host cells from activators of the alternative pathway of complement. In both mice and humans, the protein is composed of 20 homologous short consensus repeat (SCR) domains. The size of the protein suggests that portions of the structure outside the known C3b binding site (SCR 1-4) possess a significant biol. role. We have expressed the full-length cDNA of factor H in the baculovirus system and have shown that recombinant protein to be fully active. Mutants of this full-length protein have now been prepd., purified, and exmd. for cofactor activity and binding to C3b and heparin. The results demonstrate (i) that factor H has at least three sites that bind C3b, (ii) that one of these sites is located in SCR domains 1-4, as has been shown by others, (iii) that a second site exists in the domain 6-10 region, (i.v.) that a third site resides in the SCR 16-20 region, and (v) that two heparin binding sites exist in factor H, one near SCR 13 and another in the SCR 6-10 region. Functional assays demonstrated that only the first C3b site located in SCR 1-4 expresses factor I cofactor activity. Mutant proteins lacking any one of the three C3b binding sites exhibited 6- to 8-fold redns. in affinity for C3b on sheep erythrocytes, indicating that all three sites contribute to the control of complement activation on erythrocytes. The identification of multiple functionally distinct sites on factor H clarifies many of the heretofore unexplainable behaviors of this protein, including the heterogeneous binding of factor H to surface-bound C3b, the effects of trypsin cleavage, and the

differential control of complement activation on activators and nonactivators of the alternative pathway of complement.

L9 ANSWER 6 OF 46 CAPLUS COPYRIGHT 1999 ACS

ACCESSION NUMBER: 1996:252939 CAPLUS

DOCUMENT NUMBER: 124:286566

TITLE: Human skeletal myoblasts spontaneously activate allogeneic complement but are resistant to killing
AUTHOR(S): Gasque, Philippe; Morgan, B. Paul; Legodec, Jocelyne;

Chan, Philippe; Fontaine, Marc

CORPORATE SOURCE: Dep. Med. Biochem., Univ. Wales Coll. Med., Cardiff, UK

SOURCE: J. Immunol. (1996), 156(9), 3402-11
CODEN: JOIMA3; ISSN: 0022-1767

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The complement (C) system has previously been implicated in several

diseases of muscle. We here report that human myoblasts or rhabdomyosarcoma cell lines spontaneously activate C through the classical

pathway, causing release of anaphylatoxins and coating of

myoblasts with

opsonic C fragments but without causing cell killing. Survival of myoblasts is a consequence of the abundant expression of the membrane C

regulatory mols. MCP and CD59, and neutralization of CD59

renders cells

susceptible to C killing. The decay-accelerating factor was

expressed at

a very low level. Myoblasts and rhabdomyosarcoma lines also abundantly

express the fluid-phase regulators C1-inhibitor, factor H, C4

binding

protein, S-protein, and clusterin and secrete a sol. form of CD59.

Expression of membrane and fluid-phase regulators is enhanced by either

IFN-gamma, or TNF-alpha.. Although myoblasts resist C killing, spontaneous activation of C on these cells may have important consequences

in inflammatory diseases of muscle where the generation of anaphylactic

and opsonic fragments with recruit and activate inflammatory

cells. C

activation on myoblasts may also have consequences for the use of these

cells as vehicles for gene delivery. Inhibition of C using sol.

complement receptor 1 (sCR1) efficiently protected myoblasts

from C attack

in vitro, and this agent, already being tested in therapy of several

C-mediated diseases, might be of value in inflammatory muscle

disease and

in improving the efficiency of gene delivery.

L9 ANSWER 7 OF 46 CAPLUS COPYRIGHT 1999 ACS

ACCESSION NUMBER: 1996:708713 CAPLUS

DOCUMENT NUMBER: 126:6135

TITLE: Complement regulatory protein expression by a human

oligodendrocyte cell line: cytokine regulation and comparison with astrocytes

AUTHOR(S): Gasque, P.; Morgan, B. P.

CORPORATE SOURCE: Dep. of Medical Biochemistry,

Tenovus Building,

Cardiff, CF4 4XX, UK

SOURCE: Immunology (1996), 89(3), 338-347

CODEN: IMMUAM; ISSN: 0019-2805

PUBLISHER: Blackwell

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Rat oligodendrocytes spontaneously active complement (C) and lack the C

inhibitor CD59. As a consequence, rat oligodendrocytes are

susceptible to

lysis by autologous C in vitro. Expression of C inhibitors on

human

oligodendrocytes in vitro and other human glia has yet to be well

characterized. We have previously shown expression at the

mRNA level of

the membrane inhibitors CD59, decay-accelerating factor (DAF;

CD55) and

membrane cofactor protein (MCP; CD46) in human astrocytes.

We here

examine the expression of membrane and secreted C inhibitors by the

oligodendrocyte cell line, HOG. HOG cells abundantly express

CD59,

assessed at protein and mRNA level, and expressed CAF and

MCP, albeit at a

lower level. Expression of all three inhibitors was enhanced by

incubation with interferon-gamma, or with phorbol ester (PMA).

Complement receptor type I (***CR1*** ; ***CD35***)

was neither

expressed constitutively nor induced by cytokines. HOG also

constitutively secreted C1-inhibitor, S-protein and clusterin.

Factor H

was secreted only after stimulation with cytokines. C4b binding

proteins

was expressed at a very low level and was detected only at the mRNA level
by reversed transcriptase-polymerase chain reaction (RT-PCR).

For comparison, astrocyte expression of CD59, DAF, MCP and ***CR1*** was confirmed at the mRNA and protein levels. HOG did not activate C spontaneously, as judged by the lack of deposition of C fragments, and were not lysed by C even after inhibition of CD59 and DAF using specific monoclonal antibodies.

L9 ANSWER 8 OF 46 CAPLUS COPYRIGHT 1999 ACS

ACCESSION NUMBER: 1995:538616 CAPLUS

DOCUMENT NUMBER: 122:263536

TITLE: Chimeric proteins which block complement activation

INVENTOR(S): Ko, Jone Long; Higgins, Paul J.; Yeh, C. Grace

PATENT ASSIGNEE(S): Cytomed, Inc., USA

SOURCE: PCT Int. Appl., 73 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO.
DATE

WO 9508570 A1 19950330 WO 94-US10786 19940923

W: AU, CA, CN, JP
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

US 5679546 A 19971021 US 94-310416 19940922

AU 9480719 A1 19950410 AU 94-80719 19940923

AU 697167 B2 19981001

EP 723555 A1 19960731 EP 94-931763 19940923

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE

JP 09502985 T2 19970325 JP 94-509957 19940923

PRIORITY APPLN. INFO.: US 94-310416 19940922
US 93-126596 19930924

US 94-310416 19940922
WO 94-US10786 19940923

AB The present invention relates to novel chimeric proteins comprising a

first and a second polypeptides which inhibit complement activation,

linked to a second polypeptide which inhibits complement activation

selecting from membrane cofactor protein (MCP), decay

accelerating factor (DAF), complement receptor 1, factor H, C4b binding protein, or fragments.

Nucleic acids encoding the novel chimeric proteins and methods for

purifying the chimeric proteins and reducing inflammation with the

administration of the chimeric proteins of the invention. In

example, a recombinant gene encoding a complement receptor fusion

proteins, e.g., MCP-MCP, MCP-DAF and DAF-MCP were mol. cloned and

expressed, and a complement activation blocker, CAB-2, was purified and identified

by ELISA. The protein cofactor and decay accelerating factor

activities were confirmed and inhibition of complement-mediated lysis was tested.

L9 ANSWER 9 OF 46 CAPLUS COPYRIGHT 1999 ACS

ACCESSION NUMBER: 1995:643347 CAPLUS

DOCUMENT NUMBER: 123:54150

TITLE: Modified truncated complement system regulators for

autoimmune disease treatment, transplant rejection

suppression, or tissue damage diagnosis

INVENTOR(S): Atkinson, John P.; Hourcade, Dennis; Krych, Małgorzata

PATENT ASSIGNEE(S): Washington University, USA

SOURCE: PCT Int. Appl., 74 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO.
DATE

WO 9508343 A1 19950330 WO 94-US10820 19940923

W: AU, CA, JP
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

CA 2171953 AA 19950330 CA 94-2171953 19940923

AU 9478424 A1 19950410 AU 94-78424 19940923

AU 691525 B2 19980521

EP 730469 A1 19960911 EP 94-929330 19940923

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE

JP 09506764 T2 19970708 JP 94-509968 19940923

PRIORITY APPLN. INFO.: US 93-126505 19930923

WO 94-US10820 19940923

AB Analogs of regulators of complement activation (RCA) proteins which have

altered specificities and affinities for the targets C3b and/or C4b

are described. These analogs are obtained by substituting amino acids

which affect the complement inhibitory activities of these proteins,

substituting, rearranging or adding short consensus repeats (SCRs)

or SCR regions to the proteins, deleting amino acid sequences, and

combinations thereof.

L9 ANSWER 10 OF 46 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 95181440 EMBASE

DOCUMENT NUMBER: 1995181440

TITLE: Evaluation of the relationship between protein S and C4b-binding protein isoforms in hereditary protein S deficiency demonstrating type I and type III deficiencies to be phenotypic variants of the same genetic disease.

AUTHOR: Zoller B.; Garcia de Frutos P.; Dahlback B.

CORPORATE SOURCE: Department of Clinical Chemistry, Malmö General Hospital, S-20502 Malmö, Sweden

SOURCE: Blood, (1995) 85(12) (3524-3531).

ISSN: 0006-4971 CODEN: BLOOWA

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 022 Human Genetics

025 Hematology

037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Type III protein S deficiency is characterized by a low plasma level of

free protein S, whereas the total concentration of protein S is normal. In

contrast, both free and total protein S levels are low in type I deficiency. To elucidate the molecular mechanism behind the selective

deficiency of free protein S in type III deficiency, the relationship between the plasma concentrations of beta-chain containing isoforms of

C4b-binding protein (***C4BP*** .beta.+) and different forms of protein

S (free, bound, and total) was evaluated in 327 members of 18 protein S-deficient families. In normal relatives (n = 190), protein S correlated

well with ***C4BP*** .beta.+ with free protein S (96 .+-. 23 nmol/L)

being equal to the molar excess of protein S (355 .+-. 65 nmol/L) over

C4BP .beta.+ (275 .+-. 47 nmol/L). In protein S-deficient family

members (n = 117), the equimolar relationship between protein S (215 .+-.

50 nmol/L) and ***C4BP*** .beta.+ (228 .+-. 51 nmol/L), together with

the high affinity of the interaction, resulted in low levels of free protein S (16 .+-. 10 nmol/L). Free protein S levels were distinctly low

in protein S-deficient members, whereas in 47 of the protein S-deficient individuals, the concentration of total protein S was within the normal

range, which fulfills the criteria for type III deficiency. The remaining

70 had low levels of both total and free protein S and, accordingly, would

be type I deficient. Coexistence of type I and type III deficiency was

found in 14 families, suggesting the two types of protein S deficiency to

be phenotypic variants of the same genetic disease. Interestingly, not

only protein S but also ***C4BP*** .beta.+ levels were decreased in

orally anticoagulated controls and even more so in anticoagulated protein

S- deficient members, suggesting that the concentration of

C4BP .beta.+ is influenced by that of protein S. In conclusion, our results

indicate that type I and type III deficiencies are phenotypic

variants of the same genetic disease and that the low plasma concentrations of free

protein S in both types are the result of an equimolar relationship between protein S and ***C4BP*** .beta.+.

L9 ANSWER 11 OF 46 MEDLINE DUPLICATE 1

ACCESSION NUMBER: 95226458 MEDLINE

DOCUMENT NUMBER: 95226458

TITLE: cDNA structure of rabbit C4b-binding protein alpha-chain.
ALPHA-CHAIN: Preserved sequence motive in complement regulatory protein modules which bind C4b.
AUTHOR: Garcia de Frutos P; Dahlback B
CORPORATE SOURCE: Department of Clinical Chemistry, University of Lund, Malmo General Hospital, Sweden.
SOURCE: BIOCHIMICA ET BIOPHYSICA ACTA, (1995 Apr 4) 1261 (2) 285-9.
 Journal code: AOW. ISSN: 0006-3002.
PUB. COUNTRY: Netherlands
 Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
OTHER SOURCE: GENBANK-Z35490
ENTRY MONTH: 199507
AB A full length cDNA clone for the alpha-chain of the rabbit complement regulatory protein C4b-binding protein (***C4BP***) was isolated from a liver cDNA library. The clone encoded an open reading frame of 597 amino acids, which included a signal peptide, eight short consensus repeats (SCR) and a carboxy terminal non-repeat region. Gel filtration of rabbit plasma and testing of fractions for factor I cofactor activity (***C4BP*** -like) revealed two peaks of activity, the one with highest molecular weight corresponding in size to that of human C4b-binding protein. Comparison of the rabbit ***C4BP*** alpha-chain sequence with other SCR containing C3b/C4b binding proteins revealed highest sequence similarities between the second SCRs in ***C4BP*** from rabbit, human and murine species and SCRs at corresponding position in complement receptor 1 (***CR1***) whereas in decay accelerating factor (DAF), the third SCR was most similar. A conserved sequence motive was identified in these C4b-binding SCRs.

L9 ANSWER 12 OF 46 SCISEARCH COPYRIGHT 1999 ISI (R)
ACCESSION NUMBER: 95:258922 SCISEARCH
THE GENUINE ARTICLE: QQ952
TITLE: CDNA STRUCTURE OF RABBIT C4B-BINDING PROTEIN ALPHA-CHAIN - PRESERVED SEQUENCE MOTIVE IN COMPLEMENT REGULATORY PROTEIN MODULES WHICH BIND C4B
AUTHOR: DEFRUTOS P G; DAHLBACK B (Reprint)
CORPORATE SOURCE: LUND UNIV, MALMO GEN HOSP, DEPT CLIN CHEM, S-21401 MALMO, SWEDEN (Reprint); LUND UNIV, MALMO GEN HOSP, DEPT CLIN CHEM, S-21401 MALMO, SWEDEN
COUNTRY OF AUTHOR: SWEDEN
SOURCE: BIOCHIMICA ET BIOPHYSICA ACTA-GENE STRUCTURE AND EXPRESSION, (04 APR 1995) Vol. 1261, No. 2, pp. 285-289.
 ISSN: 0167-4781.
DOCUMENT TYPE: Note; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 26
 ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB A full length cDNA clone for the alpha-chain of the rabbit complement regulatory protein C4b-binding protein (***C4BP***) was isolated from a liver cDNA library. The clone encoded an open reading frame of 597 amino acids, which included a signal peptide, eight short consensus repeats (SCR) and a carboxy terminal non-repeat region. Gel filtration of rabbit plasma and testing of fractions for factor I cofactor activity (***C4BP*** -like) revealed two peaks of activity, the one with highest molecular weight corresponding in size to that of human C4b-binding protein. Comparison of the rabbit ***C4BP*** alpha-chain sequence with other SCR containing C3b/C4b binding proteins revealed highest sequence similarities between the second SCRs in ***C4BP*** from rabbit, human and murine species and SCRs at corresponding position in complement receptor 1 (***CR1***) whereas in decay accelerating factor (DAF), the third SCR was most similar. A conserved sequence motive was identified in

these C4b-binding SCRs.

L9 ANSWER 13 OF 46 BIOSIS COPYRIGHT 1999 BIOSIS
ACCESSION NUMBER: 1995:381172 BIOSIS
DOCUMENT NUMBER: PREV199598395472
TITLE: A soluble multimeric C3b/C4b receptor (***CR1*** , ***CD35***) using a general purpose C4 terminal ***C4BP*** multimerising systems.
AUTHOR(S): Oudin, S. (1); Tonye-Libby, M. (1); Goossens, D.; Gupta, N. (1); Cornillet, P. (1); Tabary, T. (1); Philbert, F. (1); Bacchi, V.; Fischer, E.; Rouger, P.; Kazatchkine, M. D.; Klatzmann, D.; Cohen, J. H. M. (1)
CORPORATE SOURCE: (1) Lab. Immunol., Pole Biomolecules, Reims, Paris France
SOURCE: 9TH INTERNATIONAL CONGRESS OF IMMUNOLOGY.. (1995) pp. 95.
 The 9th International Congress of Immunology.
 Publisher: 9th International Congress of Immunology San Francisco, California, USA.
 Meeting Info.: Meeting Sponsored by the American Association of Immunologists and the International Union of Immunological Societies San Francisco, California, USA July 23-29, 1995
DOCUMENT TYPE: Conference
LANGUAGE: English

L9 ANSWER 14 OF 46 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1995:130566 CAPLUS
DOCUMENT NUMBER: 122:4393
TITLE: Complement regulatory proteins of herpesvirus saimiri and their similarity to other complement-regulating proteins
INVENTOR(S): Fleckenstein, Bernhard; Albrecht, Jens-Christian
PATENT ASSIGNEE(S): Alexion Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 59 pp.
 CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. |
|------------|------|----------|-----------------------------------|
| WO 9416062 | A1 | 19940721 | WO 93-US672 19930112 W: CA, US |

AB Gene sequences for three complement regulatory proteins encoded within the genome of Herpesvirus Saimiri (HVS) are disclosed, namely, mCCPH, sCCPH, and HVS-15. MCCPH and sCCPH share substantial homol. with the human complement inhibitory protein factor H, ***CD35***, CD46, CD55, and ***C4bp*** which inhibit C3 convertase activity in the complement cascade. HVS-15 shares substantial homol. with the human complement inhibitory protein CD59 which inhibits formation of the membrane attack complex of the complement system. The gene sequences and corresponding proteins can be used as therapeutic agents to control the complement arm of the immune system.

L9 ANSWER 15 OF 46 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1994:280266 CAPLUS
DOCUMENT NUMBER: 120:280266
TITLE: Delivery of proteins by intermembrane transfer for preaccommodation of xenogeneic organ transplants and other purposes
INVENTOR(S): Byrne, Guerard W.; Kooyman, David Lee; Logan, John Steele
PATENT ASSIGNEE(S): DNX Biotherapeutics, Inc., USA
SOURCE: PCT Int. Appl., 107 pp.
 CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. |
|------------|------|----------|--|
| WO 9406903 | A1 | 19940331 | WO 93-US889 19930922 W: AT, AU, BB, BG, BR, BY, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, VN RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, |

NL, PT, SE,
 BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG EP 662125 A1 19950712 EP 93-922259 19930922
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC
NL, PT, SE
 JP 08501451 T2 19960220 JP 93-508379 19930922
 AU 671158 B2 19960815 AU 93-51325 19930922
 FI 9501325 A 19950509 FI 95-1325 19950321
 NO 9501074 A 19950519 NO 95-1074 19950321
PRIORITY APPLN. INFO.: US 92-948521 19920922
 WO 93-US889 19930922
AB GPI-linked proteins are transferred, esp. in vivo, from vertebrate carrier cells to cells of a target vertebrate tissue. For example, for purposes of xenogeneic transplantation, cells bearing complement inhibition factor(s) specific for the recipient species, e.g., genetically engineered red blood cells, are incubated with transplantable cells of a second, discordant donor species until transfer of the factor(s) occurs. The transfer may occur in vivo or in vitro, and the factor-bearing cells may be normal cells of the recipient species, or genetically engineered cells of the donor species which express a gene encoding a complement inhibition factor(s) of the recipient species, e.g., DAF, CD59, or others. The method is particularly useful in modifying pig organs (kidney, heart, etc.) for xenotransplantation into humans.

L9 ANSWER 16 OF 46 MEDLINE
ACCESSION NUMBER: 93315479 MEDLINE
DOCUMENT NUMBER: 93315479
TITLE: The human C4b-binding protein beta-chain gene.
AUTHOR: Hillarp A; Pardo-Manuel F; Ruiz R R; Rodriguez de Cordoba S; Dahlback B
CORPORATE SOURCE: Department of Clinical Chemistry, University of Lund, Malmo General Hospital, Sweden.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1993 Jul 15) 268 (20) 15173-23.
 Journal code: HIV. ISSN: 0021-9258.
PUB. COUNTRY: United States
 Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
OTHER SOURCE: GENBANK-L11244; GENBANK-L11245;
 GENBANK-L11246
ENTRY MONTH: 199310
AB Human complement component C4b-binding protein (***C4BP***) is composed of seven alpha-chains and one beta-chain. The alpha-and beta-chains are homologous and both contain multiple copies of short consensus repeats (SCR) and in addition carboxy-terminal non-repeat regions. Each of the alpha-chains contains a binding site for C4b, whereas the beta-chain binds protein S, a vitamin K-dependent protein involved in the regulation of blood coagulation. The alpha- and beta-chain genes are closely linked in the regulators of complement activation gene cluster on the long arm of human chromosome 1, band 1q32. The human beta-chain gene which has now been characterized was found to span more than 10 kilobases of DNA. The presence of at least two different beta-chain gene transcripts was suggested by the isolation of two new cDNA clones which contained different sequences in their extended 5'-untranslated regions. Northern blot analysis demonstrated that the two clones represented distinct beta-chain mRNAs with different 5' end sequences. One class of beta-chain mRNA (denoted A19) was found to be encoded by six exons and primer extension, and S1 nuclease protection assays revealed multiple 5'-untranslated spaced transcription start sites for this mRNA class. Its 5'-untranslated region and signal peptide was encoded by the first exon. The second class of mRNA (denoted A12) had a different transcription start site and its 5'-untranslated region was derived from at least three exons out of which the last one was formed by utilization of an acceptor splice site within the first A19 exon. Exons encoding the mature beta-chain and the 3'-untranslated region were common to both classes of mRNA. The beta-chain contains three SCRs, out of which the first and second are encoded by

individual exons, whereas two exons encode the third SCR. The exon encoding the carboxyl-terminal part of the third SCR also encodes 14 amino acids of the non-repeat region. The last exon encodes the remaining 46 carboxyl-terminal amino acids and the entire 3'-untranslated region. The elucidation of the organization of the beta-chain gene provides insight into the sophisticated molecular structure of ***C4BP*** and a basis for future structural and functional studies.

L9 ANSWER 17 OF 46 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 92144596 MEDLINE
DOCUMENT NUMBER: 92144596
TITLE: Segment spanning residues 727-768 of the complement C3 sequence contains a neoantigenic site and accommodates the binding of ***CR1***, factor H, and factor B.
AUTHOR: Becherer J D; Alsenz J; Esparza I; Hack C E;
Lambris J D
CORPORATE SOURCE: Basel Institute for Immunology, Switzerland.
SOURCE: BIOCHEMISTRY, (1992 Feb 18) 31 (6) 1787-94.
Journal code: A0G. ISSN: 0006-2960.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199205
AB ***CR1***, CR2, DAF, MCP, factor H, ***C4bp***, factor B, and C3
are members of a family of structurally related molecules, the majority of which belong to the complement system. Several of these molecules also share functional features such as cofactor and decay/dissociation activity and compete with one another in binding to C3b. Since factor H appears to bind to multiple sites in C3, we investigated the relationship between the factor H- and ***CR1***-binding sites in C3b. Factor H binding to C3b is inhibited by either the C3c or C3d fragments, and addition of both fragments together augments this inhibition. One monoclonal antibody, anti-C3c, which recognizes a neoantigenic epitope expressed upon cleavage to C3 to C3b, inhibited both factor H and ***CR1*** binding to EC3b cells. This monoclonal antibody (MoAb) also inhibited factor B binding to EC3b. Two observations further supported our hypothesis that these molecules bind to proximal sites in C3b. First, a synthetic peptide spanning this region of C3b (C3(727-768)) inhibited factor H binding. Second, antibodies raised against this peptide inhibited binding to ***CR1***, factor H, and factor B to C3b. These data show that H binds to at least two sites in C3b: the site in the C3c fragment is within the identified ***CR1***-binding domain while the site in the C3d fragment surrounds the CR2-binding site. (ABSTRACT TRUNCATED AT 250 WORDS)

L9 ANSWER 18 OF 46 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1992:649734 CAPLUS
DOCUMENT NUMBER: 117:249734
TITLE: Complement activation in the follicular light zone of human lymphoid tissues
AUTHOR(S): Yamakawa, M.; Imai, Y.
CORPORATE SOURCE: Sch. Med., Yamagata Univ., Yamagata, 900-23, Japan
SOURCE: Immunology (1992), 76(3), 378-84
CODEN: IMMUAM; ISSN: 0019-2805
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A comparative immunohistochem. study of the distribution pattern of complement components and regulatory proteins within secondary lymphoid follicles was performed by the immunoperoxidase technique. Fifteen lymphoid tissues including appendices, Peyer's patches and tonsils were analyzed. Sixty secondary lymphoid follicles with evident polarity, i.e., the distinct coexistence of a light zone, dark zone and mantle zone in the same lymphoid follicle, were tested with single antibodies. The

light zones were consistently immunostained in a dendritic meshwork pattern with all antibodies. The immunostaining patterns were classified into two major groups based on the immunoreactivity of the dark zone. One immunostaining pattern was characterized by no immunostaining of the dark zone to the majority of the antigens. The second group was characterized by a diffusely weak to moderate dendritic meshwork pattern of the dark zone to some immunostaining for C9 (monoclonal), S-protein, and DF-DRC1, and all immunostaining of ***CR1*** (***CD35***), Ber-Mac-DRC (***CD35***), CR2(CD21), and R4/23. All four complement regulatory proteins were localized by immunoelectron microscopy attached to the cell surface of the cells, including follicular dendritic cells, in the light zone. The data indicate that there is an evident functional difference between the light zone and the dark zone, and that complete activation of the complement system occurs only in the light zone.

L9 ANSWER 19 OF 46 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 92155718 MEDLINE
DOCUMENT NUMBER: 92155718
TITLE: Analysis of the human regulators of complement activation (RCA) gene cluster with yeast artificial chromosomes (YACs).

AUTHOR: Hourcade D; Garcia A D; Post T W; Taillon-Miller P; Holers V M; Wagner L M; Bora N S; Atkinson J P
CORPORATE SOURCE: Howard Hughes Medical Institute Laboratories, Washington University School of Medicine, St. Louis, Missouri 63110.
SOURCE: GENOMICS, (1992 Feb) 12 (2) 289-300.
Journal code: GEN. ISSN: 0888-7543.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK; GENBANK-M73721; GENBANK-M73722; GENBANK-M73448; GENBANK-M73449; GENBANK-M73450; GENBANK-M73451; GENBANK-M73452; GENBANK-M73453; GENBANK-M73454
ENTRY MONTH: 199205
AB The human regulators of complement activation gene cluster (RCA cluster)

have been partially characterized with yeast artificial chromosomes (YACs). While the data confirm many points previously elucidated, the finer resolution of YAC mapping has allowed the discovery and/or localization of partial gene duplications, the determination of gene orientations, and the measurement of gaps between known genes.

Here nine overlapping YACs that encompass a genomic region of 800 kb, encoding four RCA genes and three gene-like elements, are described. The encoded genes and two of the gene-like elements share the same orientation and are ordered (5' to 3') DAF, CR2, ***CR1***, MCP-like, ***CR1***-like, and MCP. A ***C4bp***-like region lies upstream from DAF and is likely to correspond to one recently observed by F. Pardo-Manuel, J. Rey-Campos, A. Hillarp, B. Dahlback, and S. Rodriguez de Cordoba (1990, Proc. Natl. Acad. Sci. USA 87: 4529-4533). MCP-like, a new genetic element, was discovered and found to be homologous to the 5' portion of the MCP gene.

Two large gaps of 85 kb (between CR2 and DAF) and 110 kb (between DAF and the ***C4bp***-like element) could carry additional RCA genes. The arrangement of ***CR1***, MCP-like, ***CR1***-like, and MCP, in that order, strongly suggests that this region was generated by a single duplication of neighboring ***CR1*** / ***CR1***-like and MCP/MCP-like forerunners. The RCA YACs will now serve as convenient DNA sources for the subcloning and further characterization of this region.

L9 ANSWER 20 OF 46 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1992:52936 CAPLUS
DOCUMENT NUMBER: 116:52936
TITLE: C4 binding protein fusions with therapeutically

useful

proteins

INVENTOR(S): Pasek, Mark P.; Winkler, Gunther; Liu, Theresa R.
PATENT ASSIGNEE(S): Biogen, Inc., USA
SOURCE: PCT Int. Appl., 105 pp.
CODEN: PDXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO.
DATE

WO 9111461 A1 19910808 WO 91-US567 19910128
W: AU, CA, JP, US
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE
AU 9173288 A1 19910821 AU 91-73288 19910128
EP 465633 A1 19920115 EP 91-903951 19910128
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE
JP 04506460 T2 19921112 JP 91-504137 19910128
PRIORITY APPLN. INFO.: US 90-470888 19900126
WO 91-US567 19910128

AB The complement C4 binding protein (***C4bp***) is used in fusion

proteins with therapeutic proteins to ensure targeting of the fusion protein to the blood and to prolong serum half-life. In particular, the short consensus repeats of the N-terminal region are used. The primary aim is to provide ***CD4*** antigens for use in the treatment of AIDS.

A cDNA for ***C4bp*** was cloned by polymerase chain reaction amplification of the mRNA and subcloned into the animal expression vector pJOD-10. When the cloned gene was expressed in COS-7 cells a heptameric ***C4bp*** of the correct conformation but lacking the S protein-binding subunit was produced. Chimeric genes based upon this cDNA and one encoding sol. ***CD4*** antigen were constructed and expressed in COS-7 cells. The purified fusion proteins were shown to form multimers and to bind the glycoprotein gp120 of HIV in vitro. Conditioned medium from producer cells prevented syncytia formation by HIV-infected cells.

L9 ANSWER 21 OF 46 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 92017905 MEDLINE

DOCUMENT NUMBER: 92017905
TITLE: Preferential inactivation of the C5 convertase of the alternative complement pathway by factor I and membrane cofactor protein (MCP).

AUTHOR: Seya T; Okada M; Matsumoto M; Hong K S; Kinoshita T; Atkinson J P
CORPORATE SOURCE: Department of Immunology, Center for Adult Diseases Osaka, Japan

SOURCE: MOLECULAR IMMUNOLOGY, (1991 Oct) 28 (10) 1137-47.
Journal code: NG1. ISSN: 0161-5890.

PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199201

AB Human C3b bound to the ghost of sheep erythrocytes (E*) via activation of the alternative complement pathway (E*AC3b) consists of four major constituents on SDS-PAGE of 350, 260, 210 and 180 kDa. 350 kDa C3b is a dimeric form of C3b in which the alpha' chain of one C3b binds covalently to that of the other C3b. This complex is presumed to serve as a core for the alternative pathway C5 convertase. The other C3b populations are monomers complexed with membrane proteins or sugars. Using E*AC3b (C3b labeled) as a substrate, we have investigated functional properties of membrane cofactor protein (MCP), which is an integral membrane protein with C3b-binding and factor I-dependent cofactor activities. In conjunction with factor I, MCP was found to degrade the protein-bound C3b preferentially including the 350 kDa dimer. There was a similar but lesser tendency of this selective cleavage of C3b-dimer by ***CR1*** but not by factor H or ***C4bp***. In contrast to ***CR1*** and factor H,

detergent solubilization of EAC3b was required for MCP to fully express its cofactor activity for this selective degradation of C3b. We next separated the C3b dimer from the monomers and assessed their ability to assemble the alternative C5 convertase. The C3b dimer but not the monomers expressed C5 convertase activity following the addition of factors B and D. C5 and Ni2+. Kinetic analysis of the degradation of the C3b dimer by MCP and factor I suggested that only one C3b was efficiently converted to C3bi and this occurred concomitant with a decrease in C5 convertase activity. These results suggest that MCP has the ability to more efficiently interact with protein-bound C3b and that this may relate well to its preferential ability to irreversibly inactivate the C5 convertase.

L9 ANSWER 22 OF 46 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 91287723 MEDLINE
DOCUMENT NUMBER: 91287723
TITLE: Regulatory system of guinea-pig complement C3b: tests for compatibility of guinea-pig factors H and I with human factors.
AUTHOR: Seya T; Okada M; Hazeki K; Nagasawa S
CORPORATE SOURCE: Department of Immunology, Center for Adult Diseases, Osaka, Japan..
SOURCE: MOLECULAR IMMUNOLOGY, (1991 Apr-May) 28 (4-5) 375-82.

Journal code: NG1. ISSN: 0161-5890.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199110
AB Two proteins that are involved in cleavage of methylamine-treated C3 of guinea-pig origin (C3(MA)gp) have been isolated from guinea-pig serum. One of them functioned as a cofactor of human factor I (Ihu) for cleavage of C3(MA)gp and its molecular size was 150 kDa. The other was pure and able to cleave C3(MA)gp together with human factor H (Hhu). They appear to be analogous to human factors H and I in the guinea-pig and will be referred to as Hgp and Igp. Methylamine-treated human C3 [C3(MA)hu] was not a compatible substrate for Hgp or Igp: little cleavage of C3(MA)hu was observed if human factor H (Hhu) or I was substituted with the guinea-pig counterpart. C3(MA)gp, on the other hand, served as a substrate, though less efficiently, for Hhu and Igp. Human C4b-binding protein (***C4bp***) and membrane cofactor protein (MCP) as well as Hhu could participate in cleavage of C3(MA)gp by Igp or Igp. In these assays, C3(MA)gp was degraded again less efficiently than C3(MA)hu. Interestingly, human C3b/C4b receptor (***CR1***) mediated factor I-dependent cleavage of C3(MA)hu and C3(MA)gp to a similar extent regardless the sources of factor I. These results suggest that factor I-dependent C3b regulatory system is species-specific except in the case of ***CR1*** , which may function as a cofactor irrespective of species.

L9 ANSWER 23 OF 46 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 89094254 MEDLINE
DOCUMENT NUMBER: 89094254
TITLE: Structural gene for human membrane cofactor protein (MCP)
of complement maps to within 100 kb of the 3' end of the C3b/C4b receptor gene.
AUTHOR: Bora N S; Lublin D M; Kumar B V; Hockett R D; Holers V M; Atkinson J P
CORPORATE SOURCE: Howard Hughes Medical Institute Laboratories, Washington University School of Medicine, St. Louis, Missouri 63110. CONTRACT NUMBER: RO1-AI19642 (NIAID)
SOURCE: JOURNAL OF EXPERIMENTAL MEDICINE, (1989 Feb 1) 169 (2) 597-602.
Journal code: I2V. ISSN: 0022-1007.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 198904
AB The structural gene for membrane cofactor protein (MCP), a widely distributed C3b/C4b binding regulatory glycoprotein of the complement system, has been mapped to the same locus as the structural genes for ***CR1*** , CR2, DAF, and ***C4bp*** . The order of the genes within an approximately 800-kb DNA fragment on the long arm of chromosome 1 is MCP- ***CR1*** -CR2-DAF- ***C4bp*** . Further, the MCP gene maps to within 100 kb of 3' end of the ***CR1*** gene.

L9 ANSWER 24 OF 46 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 89277343 EMBASE
DOCUMENT NUMBER: 1989277343
TITLE: Complexity of MHC class III genes and complement polymorphism.
AUTHOR: Rittner C.; Schneider P.M.
CORPORATE SOURCE: Institut für Rechtsmedizin, Johannes Gutenberg-Universität, 6500 Mainz, Germany
SOURCE: Immunology Today, (1989) 10/12 (401-403). ISSN: 0167-4919 CODEN: IMTOD8
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Journal
FILE SEGMENT: 022 Human Genetics
026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English
AB In July, a comparatively small group of geneticists from 23 countries met, first in Mainz and again in Berlin at the Immunology Congress, to have a closer look at the major histocompatibility complex (MHC) class III genes and other complement polymorphisms. Class III genes include not only complement but also other loci, like 21-hydroxylase (21-OH) A and B, tumour necrosis factor (TNF) .alpha. and .beta., and duplicated genes of heat shock protein 70 (HSP70), with no obvious functional relationship. On the other hand, complement loci are also found on chromosome 1 (H, ***C4B*** , ***CR1*** , C8A and B), chromosome 9 (C8G; J. Sodetz, Columbia), and chromosome 19 (C3). Curiously enough, MHC-linked complement genes still attract most attention, probably because evolution, deficiency and disease seem to have a causal relationship. These observations have been the subject of speculations from both the neutralist (J. Klein, Tubingen) and selectionist (T. Meo, Paris) point of view.

L9 ANSWER 25 OF 46 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 88187597 MEDLINE
DOCUMENT NUMBER: 88187597
TITLE: Organization of the genes encoding complement receptors type 1 and 2, decay-accelerating factor, and C4-binding protein in the RCA locus on human chromosome 1.
AUTHOR: Carroll M C; Alicot E M; Katzman P J; Klickstein L B; Smith J A; Farrow D T
CORPORATE SOURCE: Department of Pediatrics, Harvard Medical School, Boston, Massachusetts 02115.
CONTRACT NUMBER: AI-22833 (NIAID)
SOURCE: JOURNAL OF EXPERIMENTAL MEDICINE, (1988 Apr 1) 167 (4) 1271-80.
Journal code: I2V. ISSN: 0022-1007.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 198807
AB The organization and physical linkage of four members of a major complement locus, the RCA locus, have been determined using the technique of pulsed field gradient gel electrophoresis in conjunction with Southern blotting. The genes encoding ***CR1*** , CR2, DAF, and ***C4bp*** were aligned in that order within a region of 750 kb. In addition, the 5' to 3' orientation of the ***CR1*** gene (5' proximal to CR2) was determined using 5'- and 3'-specific DNA probes. The proximity of these genes may be related to structural and functional homologies of the protein products. Overall, a restriction map including 1,500 kb of DNA was

prepared, and this map will be important for positioning of additional coding sequences within this region on the long arm of chromosome 1.

L9 ANSWER 26 OF 46 MEDLINE DUPLICATE 8
ACCESSION NUMBER: 88171282 MEDLINE
DOCUMENT NUMBER: 88171282
TITLE: Structure of the human B lymphocyte receptor for C3d and the Epstein-Barr virus and relatedness to other members of the family of C3/C4 binding proteins [published erratum appears in J Exp Med 1988 Nov 1;168(5):1953-4].
AUTHOR: Weis J J; Toothaker L E; Smith J A; Weis J H; Farrow D T
CORPORATE SOURCE: Department of Rheumatology and Immunology, Brigham and Women's Hospital, Boston, Massachusetts.
CONTRACT NUMBER: AM-35907 (NIADDK)
AI-23401 (NIAID)
AI-22833 (NIAID)
+
SOURCE: JOURNAL OF EXPERIMENTAL MEDICINE, (1988 Mar 1) 167 (3) 1047-66.
Journal code: I2V. ISSN: 0022-1007.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
OTHER SOURCE: GENBANK-Y00649
ENTRY MONTH: 198807
AB Human complement receptor type 2 (CR2) is the B lymphocyte receptor for C3d and the Epstein-Barr virus. This protein is also a member of a family of C3b/C4b binding proteins that regulate complement activation, comprise tandemly repeated 60-75 amino acid sequences, and whose genes map to band q32 on chromosome 1. Overlapping cDNA clones encoding the entire human CR2 protein have been isolated from a human tonsillar cDNA library. The derived amino acid sequence of 1,032 residues encodes a peptide of 112,716 mol wt. A signal peptide was identified, followed by 15 copies of the short consensus repeat (SCR) structure common to the C3/C4 binding protein family. The entire extracellular portion of the protein comprised SCRs, thus, the ligand binding sites both for C3d and the EBV protein gp350/220 are positioned within this structure. Immediately following the final SCR was a transmembrane sequence of 24 amino acids and a cytoplasmic region of 34 amino acids. One of five cDNA clones isolated contained an additional SCR, providing evidence for alternative mRNA splicing or gene products of different human alleles. The CR2 cDNAs were used to isolate CR2-specific genomic phage. The entire CR2 coding sequences were found within 20 kb of human DNA. Analysis of the CR2 cDNA sequence indicated that CR2 contained internally homologous regions and suggested that CR2 arose by duplication of a primordial gene sequence encoding four SCRs. Comparison of the CR2 peptide sequence with those of other members of the gene family has identified many regions highly homologous with human ***CR1*** , fewer with ***C4bp*** and decay accelerating factor, and very few with factor H, and suggested that CR2 and ***CR1*** arose by duplication of the same ancestral gene sequence. The homology between CR2 and ***CR1*** extended to the transmembrane and cytoplasmic regions, suggesting that these sequences were derived from a common membrane-bound precursor.
L9 ANSWER 27 OF 46 MEDLINE DUPLICATE 9
ACCESSION NUMBER: 89127291 MEDLINE
DOCUMENT NUMBER: 89127291
TITLE: Structural and functional relationships among receptors and regulators of the complement system.
AUTHOR: Dierich M P; Schulz T F; Eigentler A; Huemer H; Schwable W
CORPORATE SOURCE: Institut für Hygiene, University of Innsbruck, Austria.
SOURCE: MOLECULAR IMMUNOLOGY, (1988 Nov 25 (11) 1043-51. Ref: 90

Journal code: NG1. ISSN: 0161-5890.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 198905
AB The classical and alternative pathway of complement activation are regulated by a series of fluid phase and cell-bound factors, some of which at the same time serve as receptors for fragments of C3 and C4. These molecules are factor H, ***CR1*** (C3b/C4b receptor), CR2 (C3d/EBV receptor), ***C4BP*** (C4b binding protein), DAF (decay accelerating factor), MCP (membrane cofactor protein; earlier designated p45/70), CR3 (iC3b receptor or Mac-1) and CR4 (protein 150/95). Due to structural, genetic and functional features these factors are members of one or several newly recognized large families of proteins: (1) molecules with 60 amino acids long repeats (H, ***CR1***, CR2, ***C4BP***, DAF); (2) proteins with 1,2-diacylglycerol membrane anchoring (DAF); (3) proteins with a heterodimer structure and preference for ligands containing the tripeptide arginine-glycine-asparagine (CR3, CR4). Recognizing the above mentioned regulators and receptors of the complement system as belonging to these protein families opens new perspectives for further genetic and functional research of mutual interest to complement and noncomplement scientists.

L9 ANSWER 28 OF 46 MEDLINE DUPLICATE 10
ACCESSION NUMBER: 88154754 MEDLINE
DOCUMENT NUMBER: 88154754
TITLE: A physical map of the human regulator of complement activation gene cluster linking the complement genes ***CR1***, CR2, DAF, and ***C4BP***.
AUTHOR: Rey-Campos J; Rubinstein P; Rodriguez de Cordoba S
CORPORATE SOURCE: Department of Immunogenetics, New York Blood Center 10021.
CONTRACT NUMBER: DK-19631-11 (NIDDK)
SOURCE: JOURNAL OF EXPERIMENTAL MEDICINE, (1988 Feb 1) 167 (2) 664-9.
Journal code: I2V. ISSN: 0022-1007.

PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 198806
AB We report the organization of the human genes encoding the complement components C4-binding protein (***C4BP***), C3b/C4b receptor (***CR1***), decay accelerating factor (DAF), and C3d receptor (CR2) within the regulator of complement activation (RCA) gene cluster. Using pulsed field gel electrophoresis analysis these genes have been physically linked and aligned as ***CR1*** -CR2-DAF- ***C4BP*** in an 800-kb DNA segment. The very tight linkage between the ***CR1*** and the ***C4BP*** loci, contrasted with the relative long DNA distance between these genes, suggests the existence of mechanisms interfering with recombination within the RCA gene cluster.

L9 ANSWER 29 OF 46 MEDLINE DUPLICATE 11
ACCESSION NUMBER: 89151487 MEDLINE
DOCUMENT NUMBER: 89151487
TITLE: The molecular genetics of components of the complement system.
AUTHOR: Campbell R D
SOURCE: BAILLIERS CLINICAL RHEUMATOLOGY, (1988 Dec) 2 (3) 547-75.
Journal code: CRY. ISSN: 0950-3579.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198906
AB Rapid progress has been made recently on the elucidation of the

structural components of the complement system by the application of recombinant DNA techniques. The derived amino acid sequences of most of the complement proteins are now available through cDNA cloning, and significant progress has been made in the discovery of the genetic organization of the corresponding genes. The linkage of some of the complement component genes has been established through the study of phenotypic genetics. Of particular interest has been the mapping of two clusters of genes which encode proteins involved in the activation of C3, C2, C4 and factor B, three of the structural components of the classical and alternative pathway C3 convertases, are encoded by genes which map to the MHC on human chromosome 6. The linkage of the genes with each other in a 100 kb segment of DNA has been established through the isolation of overlapping cosmid clones of genomic DNA, and PFGE has defined the molecular map position of these genes within the class III region of the MHC. The regulatory proteins factor H, ***C4BP***, ***CR1*** and DAF, which are involved in the control of C3 convertase activity, are encoded by closely-linked genes (termed the regulators of complement activation or RCA linkage group) that have been mapped to human chromosome 1. PFGE has defined the linkage of the ***CR1***, ***C4BP*** and DAF genes, together with the CR2 gene in an 800 kb segment of DNA, and it is clear that this technique will eventually be applied to the molecular mapping of other complement genes in relation to their flanking loci. Polymorphism is a feature of many of the complement proteins, especially those encoded by genes in the MHC class III region. Of these, C4 is by far the most polymorphic, and differences in gene size and gene number, in addition to the functional and antigenic differences in the gene products, have been recognized. Null alleles at either of the C4 loci are rather common and may be important susceptibility factors in some HLA-associated diseases, particularly SLE. The molecular basis of complement deficiency states has begun to be elucidated. In many cases, the deficiency is not caused by a major gene deletion or rearrangement, and techniques which detect single point mutations in DNA (Cotton et al, 1988) will have to be applied to fully characterize the nature of the defect.

L9 ANSWER 30 OF 46 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 88262883 EMBASE
DOCUMENT NUMBER: 1988262883
TITLE: Coagulation factor XIII B subunit is encoded by a gene linked to the regulator of complement activation (RCA) gene cluster in man.
AUTHOR: De Cordoba S.R.; Rey-Campos J.; Dykes D.D.; McAlpine P.J.; Wong P.; Rubinstein P.
CORPORATE SOURCE: Department of Immunogenetics, New York, NY 10021, United States
SOURCE: Immunogenetics, (1988) 28/6 (452-454).
ISSN: 0093-7711 CODEN: IMNGBK
COUNTRY: Germany
DOCUMENT TYPE: Journal; Journal
FILE SEGMENT: 022 Human Genetics
026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English
AB We have performed linkage analysis to determine the genetic relationship between the loci coding for coagulation factor XIII B (F13B) and the regulator of complement activation (RCA) gene cluster, comprised of the loci encoding C3b/C4b-receptor (***CR1***), C3d/Epstein-Barr virus-receptor (CR2), decay accelerating factor (DAF), C4b-binding protein (***C4BP***), and factor H (HF), as the products of these six loci show structural similarities. Here we report that the human F13B gene is also a member of RCA gene cluster and that it maps in close proximity to

the gene encoding complement factor H.

L9 ANSWER 31 OF 46 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 88256042 MEDLINE
DOCUMENT NUMBER: 88256042
TITLE: Structure and function of a cell-associated complement regulatory protein, membrane cofactor protein (MCP).
AUTHOR: Seya T
CORPORATE SOURCE: Department of Immunology, Center for Adult Diseases, Osaka.
SOURCE: HOKKAIDO IGAKU ZASSHI. HOKKAIDO JOURNAL OF MEDICAL SCIENCE, (1988 Mar) 63 (2) 259-68.
Journal code: GA9. ISSN: 0367-6102.
PUB. COUNTRY: Japan
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198810
AB Based on evidence suggesting that human leukocytes have factor I cofactor activity that is distinct from C3b/C4b receptor (***CR1***), we purified the cofactor protein from several human leukocyte cell-lines, and its structural and functional properties assessed. This protein migrates Mr 45,000-70,000 dalton region with a broad singlet or doublet on SDS-PAGE, specifically binds to C3b and C4b, has an acidic pI around pH 4, is rich in proline in amino acid analysis, possesses both N-linked and O-linked oligosaccharides, generates iC3b by acting as a cofactor for 1-mediated C3b cleavage, and does not disassemble the C3 convertases. This protein therefore shares some common properties characteristic to complement regulatory proteins, ***CR1***, H, and C4b-binding protein (***C4bp***). In addition, the functional profile of this protein is complementary to that of decay-accelerating factor (DAF) that has been known to be a protective protein for complement-mediated cell damage. We named this protein membrane cofactor protein (MCP), and suspect that the reason DAF and MCP are widely distributed on human peripheral blood cells relates to their synergistic activity profile such that complement activation on autologous tissue is inhibited.

L9 ANSWER 32 OF 46 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 90180924 MEDLINE
DOCUMENT NUMBER: 90180924
TITLE: Molecular mapping of the HLA-linked complement genes and the RCA linkage group.
AUTHOR: Campbell R D; Dunham I; Sargent C A
CORPORATE SOURCE: MRC Immunochimistry Unit, Department of Biochemistry, University of Oxford, UK.
SOURCE: EXPERIMENTAL AND CLINICAL IMMUNOGENETICS, (1988) 5 (2-3) 81-98. Ref. 113.
Journal code: AOK. ISSN: 0254-9670.
PUB. COUNTRY: Switzerland
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199006
AB Phenotypic genetics have established linkage of the genes encoding proteins involved in the activation of the complement component C3, C2, factor B and C4, three of the structural components of the classical and alternative pathway C3 convertases, are encoded by genes which have been mapped to the class III region of the major histocompatibility complex (MHC) on human chromosome 6. The regulatory proteins factor H, ***C4BP***, ***CR1***, CR2 and DAF, which are involved in the control of C3 convertase activity, are encoded by closely linked genes, termed the regulators of complement activation (RCA) linkage group, that have been mapped to human chromosome 1. cDNA clones for all these proteins have been isolated, and this has made it possible to investigate the organization and structure of the MHC class III genes and the genes in the RCA linkage group. This short review summarizes some of the main features which have emerged from recent cloning work.

L9 ANSWER 33 OF 46 MEDLINE
ACCESSION NUMBER: 90009070 MEDLINE
DOCUMENT NUMBER: 90009070
TITLE: C3 receptors on macrophages.
AUTHOR: Law S K
CORPORATE SOURCE: Department of Biochemistry, University of Oxford, UK..
SOURCE: JOURNAL OF CELL SCIENCE. SUPPLEMENT, (1988) 9 67-97. Ref:

187
Journal code: HNG. ISSN: 0269-3518.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)

LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 199001

AB The complement receptors on macrophage are responsible for their binding and ingestion of opsonized targets. The two established receptors are ***CR1***, which recognizes C3b, and CR3, which recognizes iC3b, the natural product of C3b from cleavage by the complement control protein factor I and its cofactors. ***CR1*** belongs to a group of proteins that contain a structural element characterized by its size of 60-65 amino acids, and four conservatively positioned cysteines, which engage in a self-contained 1-3, 2-4 disulphide arrangement. This structural unit is called SCR (short consensus repeat) and is found in the complement proteins C1r, C1s, C2, factor B, factor H, ***C4BP***, DAF, MCP and CR2, each of which interacts with some cleavage products of C3 and/or C4.

CR1 has 30 SCR units accounting for its entire extracellular structure. It has a transmembrane segment and a small cytoplasmic domain. CR3 is a heterodimer containing an alpha and beta subunit held together by non-covalent forces. The beta subunit is also found in the two leukocyte antigens, LFA-1 and p150,95, which have alpha subunits distinct from that of CR3. The beta subunit contains 56 cysteine residues, 42 of which lie in a span of 256 residues immediately adjacent to the transmembrane segment.

It shares extensive sequence homology with subunits of membrane protein complexes that bind fibronectin and vitronectin, implicating that they all belong to an extended set of surface adhesion molecules not restricted to the immune system. p150,95 is also expressed on macrophages and it has iC3b binding activity. It also shares some functional properties with CR3 as an adhesion surface molecule.

L9 ANSWER 34 OF 46 MEDLINE DUPLICATE 14
ACCESSION NUMBER: 87196375 MEDLINE
DOCUMENT NUMBER: 87196375
TITLE: Expansion of the complement receptor gene family. Identification in the mouse of two new genes related to the ***CR1*** and CR2 gene family.
AUTHOR: Aegelet-Shaw M; Cole J L; Klickstein L B; Wong W W; Fearon D T; Lalley P A; Weis J H
CONTRACT NUMBER: AI-23401 (NIAID)
AI-22833 (NIAID)
AI 07323-01 (NIAID)
+
SOURCE: JOURNAL OF IMMUNOLOGY, (1987 May 15) 138 (10) 3488-94.
Journal code: IFB. ISSN: 0022-1767.

PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; Cancer Journals

OTHER SOURCE: GENBANK-M16179

ENTRY MONTH: 198708

AB Human cDNA probes encoding the C3b/C4b complement receptor, ***CR1***, have been used to identify, in the mouse, two new genes which are related to ***CR1*** but which appear to encode a different protein product. These new mouse genes, arbitrarily designated mouse genes X and Y,

hybridize specifically to three different cDNA probes derived from human ***CR1***. The degree of hybridization homology between the mouse X and Y genes suggests they are very closely related to one another; however, the chromosomal localization of the mouse X gene to chromosome 8 and the mouse Y gene to chromosome 1 indicates they are distinct gene sequences. The mRNA species detected with the X and/or Y (X/Y) sequences are approximately 2000 bases in length, but vary in both quantity and size depending upon the tissue analyzed. DNA sequence analysis of a cDNA specific for the X and Y sequences indicates the mature protein(s) will contain the 60 amino acid consensus repeat characteristic of a group of other proteins including ***CR1***, the C3d receptor (CR2), H, C4 binding protein (***C4bp***), the interleukin 2 (IL 2) receptor and others. The identity of the mouse X and Y genes, and the function of the proteins which they encode, is not known; however, the small size of the mRNA and the tissue specific expression suggests they do not encode mouse ***CR1*** or CR2 but instead encode a related protein (or proteins) which is expressed in a wide variety of mouse tissues.

L9 ANSWER 35 OF 46 MEDLINE DUPLICATE 15
ACCESSION NUMBER: 87191030 MEDLINE
DOCUMENT NUMBER: 87191030
TITLE: The superfamily of C3b/C4b-binding proteins.
AUTHOR: Kristensen T; D'Eustachio P; Ogata R T; Chung L P; Reid K B; Tack B F
CONTRACT NUMBER: AI 19222 (NIAID)
AI 22214 (NIAID)
GM 29831 (NIGMS)
SOURCE: FEDERATION PROCEEDINGS, (1987 May 15) 46 (7) 2463-9. Ref:
67
Journal code: EUV. ISSN: 0014-9446.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 198708
AB The determination of primary structures by amino acid and nucleotide sequencing for the C3b-and/or C4b-binding proteins H, ***C4BP***, ***CR1***, B, and C2 has revealed the presence of a common structural element. This element is approximately 60 amino acids long and is repeated in a tandem fashion, commencing at the amino-terminal end of each molecule. Two other complement components, C1r and C1s, have two of these repeating units in the carboxy-terminal region of their noncatalytic A chains. Three noncomplement proteins, beta 2-glycoprotein I (beta 2I), the interleukin 2 receptor (IL 2 receptor), and the b chain of factor XIII, have 4, 2 and 10 of these repeating units, respectively. These proteins obviously belong to the above family, although there is no evidence that they interact with C3b and/or C4b. Human haptoglobin and rat leukocyte common antigen also contain two and three repeating units, respectively, which have more limited homology with the repetitive regions in this family. All available data indicate that multiple gene duplications and exon shuffling have been important features in the divergence of this family of proteins with the 60-amino-acid repeat.

L9 ANSWER 36 OF 46 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1987:615904 CAPLUS
DOCUMENT NUMBER: 107:215904
TITLE: New alleles of C4-binding protein and factor H and further linkage data in the regulator of complement activation (RCA) gene cluster in man
AUTHOR(S): Rodriguez de Cordoba, S.; Rubinstein, P.
CORPORATE SOURCE: Lindsley F. Kimball Res. Inst., New York Blood Cent., New York, NY, 10021, USA
SOURCE: Immunogenetics (1987), 25(4), 267-8
CODEN: IMNGBK; ISSN: 0093-7711

DOCUMENT TYPE: Journal
LANGUAGE: English
AB By isoelec. focusing, a 3rd allele, ***C4BP*** *3, was detected for human complement C4-binding protein (***C4BP***). Also, in addn. to the 3 genetic variants of factor H, 2 new FH alleles, FH*4 and FH*5, were identified. The exclusive assocn. of the ***C4BP*** *2 allele with C3bR*B haplotypes seems to indicate that the genes coding for ***C4BP*** and ***CR1*** may be in extremely close vicinity.

L9 ANSWER 37 OF 46 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 87252916 MEDLINE
DOCUMENT NUMBER: 87252916
TITLE: Decay-accelerating factor. Genetic polymorphism and linkage to the RCA (regulator of complement activation) gene cluster in humans.
AUTHOR: Rey-Campos J; Rubinstein P; Rodriguez de Cordoba S
CONTRACT NUMBER: DK 19631-11 (NIDDK)
SOURCE: JOURNAL OF EXPERIMENTAL MEDICINE, (1987 Jul 1) 166 (1) 246-52.
Journal code: I2V. ISSN: 0022-1007.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 198710
AB We have investigated the genetic relationships between the human decay-accelerating factor (DAF) and a group of complement components including the C3b/C4b receptor (***CR1***), C4-binding protein (***C4bp***), and factor H (H), to which DAF is structurally and functionally related. ***CR1***, ***C4bp***, and H were previously demonstrated to be encoded by a cluster of closely linked genes, which we have designated regulator of complement activation (RCA). Southern blot analysis of genomic DNA using a DAF cDNA probe unraveled the existence of restriction fragment length polymorphism (RFLP) for both Bam HI and Hind III restriction endonucleases. Segregation analysis of these polymorphic fragments in families informative for the segregation of alleles at the ***CR1***, ***C4BP***, and H loci (RCA-haplotypes), demonstrated that, in humans, the gene encoding DAF is located within the RCA gene cluster. No recombinants between DAF and ***C4BP*** / ***CR1*** were encountered in 32 informative meioses. In addition, in two individuals showing recombination between the ***CR1*** / ***C4BP*** and H loci, DAF segregated with the ***CR1*** / ***C4BP*** segment. Thus, the DAF gene maps closer to the ***CR1*** / ***C4BP*** loci than to the H gene, from which it can be separated by genetic recombination.

L9 ANSWER 38 OF 46 BIOSIS COPYRIGHT 1999 BIOSIS
ACCESSION NUMBER: 1988:61486 BIOSIS
DOCUMENT NUMBER: BR34:28182
TITLE: ORGANIZATION OF THE GENES ENCODING ***CR1*** CR2 DAF AND ***C4BP*** IN THE RCA LOCUS ON HUMAN CHROMOSOME ONE.
AUTHOR(S): CARROLL M C; ALICOT E A; KATZMAN P; KLICKSTEIN L B; FEARON D T
CORPORATE SOURCE: DEP. PEDIATR., HARV. MED. SCH., BOSTON, MASS., USA.
SOURCE: XIITH INTERNATIONAL COMPLEMENT WORKSHOP, CHAMONIX, FRANCE, SEPTEMBER 18-21, 1987. COMPLEMENT, (1987) 4 (3-4), 141.
CODEN: CMPLDF. ISSN: 0253-5076.

DOCUMENT TYPE: Conference
FILE SEGMENT: BR; OLD
LANGUAGE: English

L9 ANSWER 39 OF 46 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 86183329 MEDLINE
DOCUMENT NUMBER: 86183329
TITLE: The molecular genetics of components of complement.
AUTHOR: Campbell R D; Carroll M C; Porter R R
SOURCE: ADVANCES IN IMMUNOLOGY, (1986) 38

203-44. Ref: 217

Journal code: 2N9. ISSN: 0065-2776.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 198607

AB Rapid progress has been made in establishing linkages and in chromosome allocation of the genes of some 9 complement components. In the MHC, C2,

Factor B, and two C4 or C4 related genes have been placed in some detail

in both man and mouse. The gene coding for the cytochrome

P-450

21-hydroxylase has been shown to be duplicated and immediately

3' to the

two C4 genes, though it appears to be functionally and structurally unrelated to the complement components. Thus six genes have been mapped to

this region where particular haplotypes are associated with increased

susceptibility to a number of diseases, some of which are autoimmune in

character. The complete gene structure of Factor B has been solved in man

and rapid progress is being made with the C2 and C4 genes. The structural

basis of the polymorphisms of these genes is being established. In

C4, the polymorphism is exceptionally complex with varying numbers of loci and

probably more than 50 allotypes occurring in man. A structural basis has

also been found for the big differences in the biological activity of some

of the C4 allotypes in man. Apart from the genes in the MHC, linkage has

been found between the genes coding for ***C4bp*** ,

CR1 , and

Factor H. Remarkably there are sequence homologies between these proteins

and C2 and Factor B, probably related to the ability to bind to one or

other of the structurally similar proteins C3b and C4b. The complete cDNA

sequences of C3 and C4 in mouse and man have given much information on the

many posttranslational modifications of these proteins. A partial structure has been obtained for the C3 gene and the homology shown between

C3, C4, C5, alpha 2-macroglobulin, and pregnancy zone protein.

Although the amount of detailed information in the molecular genetics of complement

components is accumulating rapidly, there appears to be a reasonable

prospect that linkages and homologies will classify the data into a comprehensible form.

L9 ANSWER 40 OF 46 MEDLINE DUPLICATE 18

ACCESSION NUMBER: 86188123 MEDLINE

DOCUMENT NUMBER: 86188123

TITLE: Partial characterization of human complement factor H by

protein and cDNA sequencing: homology with other complement

and non-complement proteins.

AUTHOR: Ripoche J; Day A J; Willis A C; Belt K T;

Campbell R D; Sim

R B

SOURCE: BIOSCIENCE REPORTS, (1986 Jan) 6 (1) 65-72.

Journal code: A6D. ISSN: 0144-8463.

PUB. COUNTRY: ENGLAND: United Kingdom

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 198608

AB Factor H, a control protein of the human complement system, is closely

related in functional activity to two other complement control proteins,

C4-binding protein (***C4bp***) and complement receptor type I (

CR1). ***C4bp*** is known to have an unusual

primary structure

consisting of eight homologous units each about 60 amino acids long. Such

units also occur in the N-terminal regions of the complement proteins C2

and factor B, and in the non-complement serum glycoprotein beta

21. Amino acid sequencing, and sequencing of a factor H cDNA clone, show that factor

H also contains internal repeating units, and is homologous to the proteins listed above.

L9 ANSWER 41 OF 46 MEDLINE

DUPLICATE 19

ACCESSION NUMBER: 85290843 MEDLINE

DOCUMENT NUMBER: 85290843

TITLE: Purification and functional analysis of the polymorphic variants of the C3b/C4b receptor (***CR1***) and comparison with H, C4b-binding protein (***C4bp***), and decay accelerating factor (DAF).

AUTHOR: Seya T; Holers V M; Atkinson J P

CONTRACT NUMBER: 5 R01-A119642

SOURCE: JOURNAL OF IMMUNOLOGY, (1985 Oct) 135 (4) 2661-7.

Journal code: IFB. ISSN: 0022-1767.

PUB. COUNTRY: United States

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; Cancer Journals

ENTRY MONTH: 198512

AB Four ***CR1*** variants have been found in the normal population and are designated ***CR1*** -A (190,000 daltons), ***CR1*** -B (220,000 daltons), ***CR1*** -C (160,000 daltons), and ***CR1*** -D (250,000 daltons).

In the present study, we first developed an improved chromatographic purification scheme for ***CR1*** that does not employ a C3b affinity step. ***CR1*** variants (A, B, and C) were then isolated, and their individual functional activity was assessed. Each possessed similar co-factor activity for I-mediated cleavage of C3(H2O), as well as for the inhibitory activity for fluid phase C3 convertases. These results indicate that, despite relatively large Mr differences, in

the purified state these three ***CR1*** variants have similar functional activities. The functional activity of ***CR1*** was also compared with ***C4bp*** , H, and decay accelerating factor (DAF) in

fluid phase assays designed to assess the inhibition of the C3 convertases

and co-factor activity. On a molar basis, ***CR1*** had approximately

the same inhibitory activity as ***C4bp*** for the classical pathway

convertase, and had the same as H for the alternative pathway convertase.

These results indicate that ***CR1*** encompasses the functional capabilities of both proteins. They also raise a number of interesting

genetic and structural questions in regard to these complement regulatory proteins, because ***C4bp*** is thought to have multiple C4b binding domains, whereas H is reported to bind one C3b. DAF was an approximately

fourfold better inhibitor of the alternative pathway convertase than ***CR1*** or H, but was a fourfold less efficient inhibitor of the classical pathway convertase than ***CR1*** or ***C4bp*** .

The effective inhibitory capacity of DAF in these fluid phase assay systems suggests that the DAF substrate specificity is for the convertases. Fluid phase ***CR1*** was twofold less efficient than H in serving as a

co-factor for the first cleavage of fluid phase C3b, and hardly mediated the second cleavage. These data are in contrast to the co-factor activity of ***CR1*** on a cell membrane, and provide additional evidence for

the local environment being a critical modulator of the function of proteins that regulate the activation of C3.

L9 ANSWER 42 OF 46 MEDLINE DUPLICATE 20

ACCESSION NUMBER: 86130416 MEDLINE

DOCUMENT NUMBER: 86130416

TITLE: Large-scale isolation of complement receptor type I (***CR1***) from human erythrocytes. Proteolytic fragmentation studies.

AUTHOR: Sin R B

SOURCE: BIOCHEMICAL JOURNAL, (1985 Dec 15) 232 (3) 883-9.

Journal code: 9Y0. ISSN: 0264-6021.

PUB. COUNTRY: ENGLAND: United Kingdom

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals; Cancer Journals

ENTRY MONTH: 198605

AB A large-scale procedure for the isolation of complement receptor type I (***CR1*** , the C3b receptor) from human erythrocytes is described. Two

of the four known phenotypes of ***CR1*** are detectable in

isolated material. Amino acid and hexosamine analysis of the A phenotype

(Mr 240 000) indicates a polypeptide chain length of about 2030

amino

acids and a carbohydrate content of 8%. Both N- and O-linked sugars appear

to be present. Trypsin digestion of isolated ***CR1*** shows that it is degraded rapidly and extensively, and no stable products of Mr greater

than 25000 are found. The ability of the receptor to bind to solid-phase

ligand is destroyed after a single cleavage by trypsin. The capacity of

the receptor to act as a cofactor for Factor I-mediated cleavage of soluble C3b is, however, only gradually decreased by proteolysis, and 30%

of this activity remains after extensive degradation. The same pattern of

loss of binding to solid-phase ligand, with partial retention of interaction with soluble ligand, is also characteristic of the complement

proteins Factor H and ***C4bp*** , which are functionally related to

CR1 .

L9 ANSWER 43 OF 46 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 85116735 EMBASE

DOCUMENT NUMBER: 1985116735

TITLE: Functional analysis of allelic variants of ***CR1*** and comparison to H, ***C4bp*** and DAF.

AUTHOR: Seya T.; Atkinson J.P.

CORPORATE SOURCE: HHMI at Washington University School of Medicine, St.

Louis, MO 63110, United States

SOURCE: Federation Proceedings, (1985) 44/4 (No. 3373).

CODEN: FEPRA7

COUNTRY: United States

DOCUMENT TYPE: Journal

FILE SEGMENT: 026 Immunology, Serology and Transplantation

LANGUAGE: English

L9 ANSWER 44 OF 46 MEDLINE DUPLICATE 2

ACCESSION NUMBER: 84214789 MEDLINE

DOCUMENT NUMBER: 84214789

TITLE: Control of the function of substrate-bound C4b-C3b by the complement receptor ***Cr1*** .

AUTHOR: Medoff M E; Nussenzweig V

CONTRACT NUMBER: AI-08499 (NIAID)

SOURCE: JOURNAL OF EXPERIMENTAL MEDICINE, (1984 Jun 1) 159 (6) 1669-85.

Journal code: I2V. ISSN: 0022-1007.

PUB. COUNTRY: United States

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals; Cancer Journals

ENTRY MONTH: 198409

AB The complement fragments C3b and C4b are the main ligands for the membrane receptor ***CR1*** . We showed elsewhere that ***CR1*** functions

as an essential cofactor for the factor I-mediated enzymatic breakdown of

membrane-bound C3b (*C3b) into C3c and * C3dg . One of the main findings of the present paper is that ***CR1*** also promotes the degradation of bound C4b (*C4b) into C4c and *C4d. On a weight basis, the cofactor

activity of ***CR1*** in the cleavage of *C4b present on the cell intermediate EAC14 is 10(3)-fold greater than that of the serum cofactor

C4-binding protein (***C4bp***). An additional finding is that the

effect of ***CR1*** on either *C3b or *C4b is modulated by the presence of the other ligand in its vicinity; that is, *C4b degradation by ***CR1*** plus I is enhanced by neighboring *C3b and vice versa. For example, upon uptake of optimal amounts of *C3b onto EAC14 and the

assembly of the C3-convertase EAC1423 , the activity of ***CR1*** in

generating C4c is enhanced 5-10 times further. Conversely, when the number of *C3b molecules on EAC1423 is relatively small (or when EAC1423 has been converted by I plus H into EAC1423i), the presence of neighboring *C4b enhances the conversion of *C3b (or *iC3b) into C3c plus * C3dg . The

enhancing effect of *C3b on the cleavage of *C4b by I is observed only if the cofactor of this reaction is ***CR1*** . Indeed, the activity

of the cofactor of this reaction is ***CR1*** .

of I or I plus ***C4bp*** on *C4b is significantly inhibited when *C3b is fixed and the main product of the reaction is *iC4b. Taken together, these findings suggest that degradation of *C4b will be more effective when enough C3b molecules are fixed nearby, thus facilitating the interaction of *C4b*3b clusters with ***CR1***-bearing cells, and that under physiological conditions, *C4b activity can be efficiently controlled by ***CR1***.

L9 ANSWER 45 OF 46 MEDLINE DUPLICATE 22
ACCESSION NUMBER: 85101648 MEDLINE

DOCUMENT NUMBER: 85101648
TITLE: Protection of the classical and alternative complement pathway C3 convertases, stabilized by nephritic factors, from decay by the human C3b receptor.

AUTHOR: Fischer E; Kazatchkine M D; Mecarelli-Halbwachs L

SOURCE: EUROPEAN JOURNAL OF IMMUNOLOGY, (1984 Dec) 14 (12) 1111-4.

Journal code: ENS. ISSN: 0014-2980.

PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals; Cancer Journals

ENTRY MONTH: 198505

AB Formation and function of the classical (C4b,2a) and alternative (C3b,Bb) complement pathway C3 convertases are regulated by the intrinsic

ability of the enzymes, extrinsic decay by ***C4bp*** and H, cleavage of C4b

and C3b by I, and by the inhibitory action of the C3b receptor molecule (***CR1***).

Binding of C4 nephritic factor (C4Nef) to C4b and of C3

nephritic factor (C3Nef) to C3b stabilizes the C3 convertases and bypasses

inactivation by ***C4bp***, H and/or I. In the present study, binding

of C4Nef to the classical C3 convertase was found to prevent

decay of

C4b,2a by inputs of ***CR1*** that were at least 15 times the amount

of ***CR1*** which inactivated 50% unstabilized classical

pathway C3

convertase sites in 2.5 min. ***CR1*** could however inhibit

lysis of

C4b,2a(C4Nef)-bearing cells in a dose-dependent manner. The latter

inhibitory effect was directed at the interaction of C5 with the C5 convertase, most likely at C5 binding to cell-bound C3b. In an

analogous manner to C4Nef in the classical pathway, stabilization of

alternative pathway C3b,Bb convertase sites by C3Nef resulted in a relative

protection of C3 convertase sites from decay by ***CR1***. Thus, C4Nef and C3Nef

can bypass all mechanisms susceptible to regulate function of the

classical and alternative pathway C3 convertases. Because

CR1 is essential for degradation of C3b bound to immune complexes in

whole blood, stabilization of C4b,2a and C3b,Bb by C4Nef and C3Nef may alter

in vivo processing of immune complexes in patients with nephritic factors.

L9 ANSWER 46 OF 46 MEDLINE DUPLICATE 23
ACCESSION NUMBER: 83162382 MEDLINE

DOCUMENT NUMBER: 83162382
TITLE: Functional properties of membrane-associated

complement receptor ***CR1***.

AUTHOR: Iida K; Nussenzweig V

CONTRACT NUMBER: AI 08499 (NIAID)

SOURCE: JOURNAL OF IMMUNOLOGY, (1983 Apr) 130 (4) 1876-80.

Journal code: IFB. ISSN: 0022-1767.

PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority

Journals

ENTRY MONTH: 198307
AB It was previously shown that membrane receptors for C3b (***CR1***)

purified from human erythrocytes were powerful inhibitors of the complement cascade and that they encompass the regulatory functions of the

serum proteins beta 1H (H) and C4-binding protein (***C4bp***).

In the present report we study the functional properties of

membrane-associated ***CR1***. When tonsil lymphocytes, which contain between

30 and 60% of

CR1-bearing B cells, are incubated with the red cell complement intermediate EAC14oxy2lim or EAC14oxy23lim, they inhibit both C42 and C423 in a dose-dependent manner. These effects are mediated by membrane-associated molecules. Indeed, mild trypsinization of the lymphocytes abolishes their activity, and formaldehyde-fixed cells are as effective as viable cells. The inhibitory effects are in part mediated by ***CR1***. The lymphocyte activities are reversed about 60% if monoclonal antibodies to ***CR1*** or fluid phase C3b are present in the incubation medium. Moreover, upon addition of C3b-inactivator (I), lymphocytes release C3c fragments from EAC14oxy23b. The release of C3c was also abolished by antibodies to ***CR1***. These results support the idea that ***CR1***, as well as other molecules from the lymphocyte membrane, can function as inhibitor(s) of complement activation in their vicinity.

=> d 110 ibib abs 1-8

L10 ANSWER 1 OF 8 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1997:267203 CAPLUS

DOCUMENT NUMBER: 126:250213
TITLE: Recombinant heteromultimeric C4 binding protein fusion

and proteins and their use for vaccines, immunotherapy

and diagnosis

INVENTOR(S): Klatzmann, David; Cohen, Jacques

PATENT ASSIGNEE(S): Universite de Reims Champagne Ardenne, Fr.; Universite Pierre et Marie Curie Paris VI

SOURCE: Fr. Demande, 36 pp.

CODEN: FRXXBL

DOCUMENT TYPE: Patent

LANGUAGE: French

FAMILY ACC. NUM. COUNT: 1

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PATENT NO. KIND DATE APPLICATION NO.
DATE

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FR 2736916 B1 19970919

WO 9704109 A1 19970206 WO 96-FR1132 19960718

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EP 842822 A1 19980520 EP 96-926424 19960718

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,

MC, PT, IE, FI

PRIORITY APPLN. INFO.: WO 95-8901 19950721

WO 96-FR1132 19960718

AB Disclosed are recombinant multimeric proteins comprising at least (a)

fusion protein A contg. C4 binding protein (***C4BP***)

alpha. chain

C-terminal residues 124-549 and a heterologous protein and (b)

fusion protein B contg. ***C4BP*** .beta. chain C-terminal residues 120-235

and a heterologous protein, the proteins A and B binding to each other

through the C-terminal domains to form the multimeric protein.

Recombinant cells producing the multimeric proteins as well as use of the

heteroolymers or cells for fetal-maternal alloimmunization, for therapy

or prophylaxis of infections, for therapy of autoimmune diseases, for

immunotherapy and for diagnosis are also disclosed. Thus,

anti-Rh(D)

scFv- ***C4BP*** and CD43 fragment- ***C4BP*** fusion

proteins were produced with CHO cells. The heteroolymeric protein formed

agglutinated

Rh+ ***erythrocytes***.

L10 ANSWER 2 OF 8 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1996:607743 CAPLUS

DOCUMENT NUMBER: 125:245269
TITLE: Identification of three physically and functionally

distinct binding sites for C3b in human ***complement*** factor H by deletion

mutagenesis

AUTHOR: Sharma, Ajay K.; Pangburn, Michael K.

CORPORATE SOURCE: Department Biochemistry, University

Texas Health Science Center, Tyler, TX, 75710-2003, USA

SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1996), 93(20),

10996-11001

CODEN: PNASA6; ISSN: 0027-8424

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Human ***complement*** factor H controls spontaneous activation of

complement in plasma and appears to play a role in distinguishing host cells from activators of the alternative pathway of ***complement***.

In both mice and humans, the protein is composed of 20 homologous short consensus repeat (SCR) domains. The size of the protein suggests that portions of the structure outside the known C3b

binding site (SCR 1-4) possess a significant biol. role. We have expressed the full-length cDNA of factor H in the baculovirus system and have shown that recombinant protein to be fully active. Mutants of this

full-length protein have now been prep'd., purified, and examd. for cofactor activity and binding to C3b and heparin. The results demonstrate (i) that factor H has at least three sites that bind C3b, (ii) that one of

these sites is located in SCR domains 1-4, as has been shown by others,

(iii) that a second site exists in the domain 6-10 region, (iv.) that a third site resides in the SCR 16-20 region, and (v) that two heparin binding sites exist in factor H, one near SCR 13 and another in the SCR

6-10 region. Functional assays demonstrated that only the first C3b site

located in SCR 1-4 expresses factor I cofactor activity. Mutant proteins

lacking any one of the three C3b binding sites exhibited 6- to 8-fold

redns. in affinity for C3b on sheep ***erythrocytes***, indicating

that all three sites contribute to the control of ***complement***.

activation on ***erythrocytes***. The identification of multiple functionally distinct sites on factor H clarifies many of the heretofore

unexplainable behaviors of this protein, including the heterogeneous

binding of factor H to surface-bound C3b, the effects of trypsin cleavage, and the differential control of ***complement*** activation on activators and nonactivators of the alternative pathway of ***complement***.

L10 ANSWER 3 OF 8 CAPLUS COPYRIGHT 1999 ACS

ACCESSION NUMBER: 1994:280266 CAPLUS

DOCUMENT NUMBER: 120:280266
TITLE: Delivery of proteins by intermembrane transfer for

and preaccommodation of xenogeneic organ transplants

other purposes

INVENTOR(S): Byrne, Guerard W.; Kooyman, David Lee; Logan, John Steele

PATENT ASSIGNEE(S): DNX Biotherapeutics, Inc., USA

SOURCE: PCT Int. Appl., 107 pp.

CODEN: PIXX2D

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO.
DATE

WO 9406903 A1 19940331 WO 93-US8889 19930922

W: AT, AU, BB, BG, BR, BY, CA, CH, CZ, DE, DK, ES, FI,

GB, HU, JP, KP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT,

RO, RU, SD, SE, SK, UA, US, VN

RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC,

NL, PT, SE, BF, BJ, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

EP 662125 A1 19950712 EP 93-922259 19930922

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC,

NL, PT, SE, JP 08501451 T2 19960220 JP 93-508379 19930922

AU 671158 B2 19960815 AU 93-51325 19930922

FI 9501325 A 19950509 FI 95-1325 19950321

NO 9501074 A 19950519 NO 95-1074 19950321

PRIORITY APPLN. INFO.: US 92-948521 19920922

WO 93-US8889 19930922

AB GPI-linked proteins are transferred, esp. in vivo, from vertebrate carrier

cells to cells of a target vertebrate tissue. For example, for

purposes of xenogeneic transplantation, cells bearing ***complement*** inhibition factor(s) specific for the recipient species, e.g., genetically

engineered red blood cells, are incubated with transplantable cells

of a

second, discordant donor species until transfer of the factor(s) occurs.

The transfer may occur in vivo or in vitro, and the factor-bearing cells

may be normal cells of the recipient species, or genetically engineered

cells of the donor species which express a gene encoding a

complement inhibition factor(s) of the recipient species, e.g.,

DAF, CD59, or others. The method is particularly useful in modifying pig

organs (kidney, heart, etc.) for xenotransplantation into humans.

L10 ANSWER 4 OF 8 MEDLINE DUPLICATE 1

ACCESSION NUMBER: 92017905 MEDLINE

DOCUMENT NUMBER: 92017905

TITLE: Preferential inactivation of the C5 convertase of the alternative ***complement*** pathway by factor I and

membrane cofactor protein (MCP).

AUTHOR: Seya T; Okada M; Matsumoto M; Hong K S; Kinoshita T;

Atkinson J P

CORPORATE SOURCE: Department of Immunology, Center for Adult Diseases Osaka, Japan.

SOURCE: MOLECULAR IMMUNOLOGY, (1991 Oct) 28 (10) 1137-47.

Journal code: NG1. ISSN: 0161-5890.

PUB. COUNTRY: ENGLAND: United Kingdom Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals; Cancer Journals

ENTRY MONTH: 199201

AB Human C3b bound to the ghost of sheep ***erythrocytes*** (E*) via activation of the alternative ***complement*** pathway

(E*AC3b)

consists of four major constituents on SDS-PAGE of 350, 260, 210 and 180

kDa. 350 kDa C3b is a dimeric form of C3b in which the alpha' chain of one

C3b binds covalently to that of the other C3b. This complex is presumed to

serve as a core for the alternative pathway C5 convertase. The other C3b

populations are monomers complexed with membrane proteins or sugars. Using

E*AC3b (C3b labeled) as a substrate, we have investigated

functional

properties of membrane cofactor protein (MCP), which is an integral

membrane protein with C3b-binding and factor I-dependent

cofactor

activities. In conjunction with factor I, MCP was found to degrade the protein-bound C3b preferentially including the 350 kDa dimer.

There was a similar but lesser tendency of this selective cleavage of C3b-dimer by

CR1 but not by factor H or ***C4bp***. In contrast to

CR1 and factor H, detergent solubilization of EAC3b

was required

for MCP to fully express its cofactor activity for this selective degradation of C3b. We next separated the C3b dimer from the monomers and

assessed their ability to assemble the alternative C5 convertase.

The C3b

dimer but not the monomers expressed C5 convertase activity following the

addition of factors B and D, C5 and Ni²⁺. Kinetic analysis of the degradation of the C3b dimer by MCP and factor I suggested that only one

C3b was efficiently converted to C3bi and this occurred

concomitant with a

decrease in C5 convertase activity. These results suggest that MCP has the

ability to more efficiently interact with protein-bound C3b and that this

may relate as well to its preferential ability to irreversibly inactivate the C5 convertase.

L10 ANSWER 5 OF 8 SCISEARCH COPYRIGHT 1999 ISI (R)

ACCESSION NUMBER: 91:397906 SCISEARCH

THE GENUINE ARTICLE: FW027

TITLE: REGULATORY SYSTEM OF GUINEA-PIG

COMPLEMENT C3B -

TESTS FOR COMPATIBILITY OF GUINEA-PIG

FACTOR-H AND

FACTOR-I WITH HUMAN-FACTORS

AUTHOR: SEYA T (Reprint); OKADA M; HAZEKI K; NAGASAWA S

CORPORATE SOURCE: CTR ADULT DIS, DEPT IMMUNOL,

HIGASHINARI KU, OSAKA 537,

JAPAN (Reprint); UNIV TOKYO, FAC

PHARMACEUT SCI, BUNKYO

KU, TOKYO 113, JAPAN; HOKKAIDO UNIV, FAC

PHARMACEUT SCI,

KITA KU, SAPPORO, HOKKAIDO 060, JAPAN

COUNTRY OF AUTHOR: JAPAN

SOURCE: MOLECULAR IMMUNOLOGY, (1991) Vol. 28,

No. 4-5, pp. 375-382

DOCUMENT TYPE: Article; Journal

FILE SEGMENT: LIFE

LANGUAGE: ENGLISH

REFERENCE COUNT: 43

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Two proteins that are involved in cleavage of methylamine-treated C3 of guinea-pig origin (C3(MA)gp) have been isolated from guinea-pig serum.

One of them functioned as a cofactor of human factor I (Hu) for cleavage of C3(MA)gp and its molecular size was 150 kDa. The other was functionally pure and able to cleave C3(MA)gp together with human factor H (Hu). They appear to be analogous to human factors H and I in the

guinea-pig and will be referred to as Hgp and Igp.

Methylamine-treated human C3 [C3(MA)hu] was not a

compatible substrate

for Hgp or Igp: little cleavage of C3(MA)hu was observed if human factor

H (Hu) or I was substituted with the guinea-pig counterpart.

C3(MA)gp

on the other hand, served as a substrate, though less efficiently, for Hu

and Igp. Human C4b-binding protein (***C4bp***) and membrane cofactor

protein (MCP) as well as Hu could participate in cleavage of C3(MA)gp by

Igp or Igp. In these assays, C3(MA)gp was degraded again less

efficiently

than C3(MA)hu. Interestingly, human C3b/C4b receptor (

CR1

mediated factor I-dependent cleavage of C3(MA)hu and

C3(MA)gp to a similar

extent regardless the sources of factor I. These results suggest that

factor I-dependent C3b regulatory system is species-specific

except in the

case of ***CR1***, which may function as a cofactor

irrespective of

species.

L10 ANSWER 6 OF 8 MEDLINE DUPLICATE 2

ACCESSION NUMBER: 86130416 MEDLINE

DOCUMENT NUMBER: 86130416

TITLE: Large-scale isolation of ***complement*** receptor type

1 (***CR1***) from human ***erythrocytes*** .

Proteolytic fragmentation studies.

AUTHOR: Sim R B

SOURCE: BIOCHEMICAL JOURNAL, (1985 Dec 15) 232

(3) 883-9.

Journal code: 9Y0. ISSN: 0264-6021.

PUB. COUNTRY: ENGLAND: United Kingdom

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals; Cancer Journals

ENTRY MONTH: 198605

AB A large-scale procedure for the isolation of ***complement*** receptor

type 1 (***CR1*** , the C3b receptor) from human

erythrocytes

is described. Two of the four known phenotypes of ***CR1***

are

detectable in the isolated material. Amino acid and hexosamine

analysis of

the A phenotype (Mr 240 000) indicates a polypeptide chain length of about

2030 amino acids and a carbohydrate content of 8%. Both N- and O-linked

sugars appear to be present. Trypsin digestion of isolated

CR1

shows that it is degraded rapidly and extensively, and no stable products

of Mr greater than 25000 are found. The ability of the receptor to bind to

solid-phase ligand is destroyed after a single cleavage by trypsin.

The

capacity of the receptor to act as a cofactor for Factor I-mediated cleavage of soluble C3b is, however, only gradually decreased by proteolysis, and 30% of this activity remains after extensive degradation.

The same pattern of loss of binding to solid-phase ligand, with partial

retention of interaction with soluble ligand, is also characteristic of the ***complement*** proteins Factor H and ***C4bp***,

which are

functionally related to ***CR1*** .

L10 ANSWER 7 OF 8 MEDLINE DUPLICATE 3

ACCESSION NUMBER: 84214789 MEDLINE

DOCUMENT NUMBER: 84214789

TITLE: Control of the function of substrate-bound C4b-C3b

by the

complement receptor ***CR1*** .

AUTHOR: Medoff M E; Nussenzweig V

CONTRACT NUMBER: AI-08499 (NIAID)

SOURCE: JOURNAL OF EXPERIMENTAL MEDICINE, (1984 Jun 1) 159 (1) 1669-85.

Journal code: I2V. ISSN: 0022-1007.

PUB. COUNTRY: United States

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals; Cancer Journals

ENTRY MONTH: 198409

AB The ***complement*** fragments C3b and C4b are the main ligands for

the membrane receptor ***CR1*** . We showed elsewhere that ***CR1***

functions as an essential cofactor for the factor I-mediated enzymatic

breakdown of membrane-bound C3b (*C3b) into C3c and *C3dg

One of the

main findings of the present paper is that ***CR1*** also promotes the

degradation of bound C4b (*C4b) into C4c and *C4d. On a weight basis, the

cofactor activity of ***CR1*** in the cleavage of *C4b present

on the

cell intermediate EAC14 is 10(3)-fold greater than that of the serum

cofactor C4-binding protein (***C4bp***). An additional finding is

that the effect of ***CR1*** on either *C3b or *C4b is modulated by

the presence of the other ligand in its vicinity; that is, *C4b degradation by ***CR1*** plus I is enhanced by neighboring *C3b and

vise versa. For example, upon uptake of optimal amounts of *C3b onto

EAC142 and the assembly of the C3-convertase EAC142, the activity of

CR1 in generating C4c is enhanced 5-10 times further. Conversely,

when the number of *C3b molecules on EAC142 is relatively small (or when

EAC142 has been converted by I plus H into EAC142i), the presence of

neighboring *C4b enhances the conversion of *C3b (or *iC3b) into *C3dg . The enhancing effect of *C3b on the cleavage of *C4b by

I is

observed only if the cofactor of this reaction is ***CR1*** .

Indeed,

the activity of I or I plus ***C4bp*** on *C4b is significantly inhibited when *C3b is fixed and the main product of the reaction is *

*C4b . Taken together, these findings suggest that degradation of *C4b

will be more effective when enough C3b molecules are fixed nearby, thus

facilitating the interaction of *C4b3b clusters with ***CR1***

-bearing cells, and that under physiological conditions, *C4b activity can

be efficiently controlled by ***CR1*** .

L10 ANSWER 8 OF 8 MEDLINE

DUPPLICATE 4

ACCESSION NUMBER: 83162382 MEDLINE

DOCUMENT NUMBER: 83162382

TITLE: Functional properties of membrane-associated

complement receptor ***CR1*** .

AUTHOR: Iida K; Nussenzweig V

CONTRACT NUMBER: AI 08499 (NIAID)

SOURCE: JOURNAL OF IMMUNOLOGY, (1983 Apr) 130

(4) 1876-80.

Journal code: IFB. ISSN: 0022-1767.

PUB. COUNTRY: United States

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority

Journals

ENTRY MONTH: 198307

AB It was previously shown that membrane receptors for C3b (

CR1)

purified from human ***erythrocytes*** were powerful

inhibitors of the

complement cascade and that they encompass the

regulatory

functions of the serum proteins beta 1H (H) and C4-binding

protein (

C4bp). In the present report we study the functional

properties of

membrane-associated ***CR1*** . When tonsil lymphocytes, which contain

between 30 and 60% of ***CR1*** -bearing B cells, are

incubated with the red cell ***complement*** intermediate EAC14oxy2lim or

EAC14oxy23lim, they inhibit both C42 and C423 in a dose-dependent manner.

These effects are mediated by membrane-associated molecules.

Indeed, mild

trypsinization of the lymphocytes abolishes their activity, and

formaldehyde-fixed cells are as effective as viable cells. The

inhibitory effects are in part mediated by ***CR1***. The lymphocyte activities are reversed about 60% if monoclonal antibodies to ***CR1*** or fluid phase C3b are present in the incubation medium. Moreover, upon addition of C3b-inactivator (I), lymphocytes release C3c fragments from EAC14oxy23b. The release of C3c was also abolished by antibodies to ***CR1***. These results support the idea that ***CR1***, as well as other molecules from the lymphocyte membrane, can function as inhibitor(s) of ***complement*** activation in their vicinity.

=> d11 ibib abs 1-2

L11 ANSWER 1 OF 2 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1997:267203 CAPLUS
DOCUMENT NUMBER: 126:250213
TITLE: Recombinant heteromultimeric C4 binding protein fusion and proteins and their use for vaccines, immunotherapy and diagnosis
INVENTOR(S): Klatzmann, David; Cohen, Jacques
PATENT ASSIGNEE(S): Université de Reims Champagne Ardennes, Fr.; Université Pierre et Marie Curie Paris VI
SOURCE: Fr. Demande, 36 pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND DATE | APPLICATION NO. |
|------------|-------------|-----------------------|
| FR 2736916 | A1 19970124 | FR 95-8901 19950721 |
| FR 2736916 | B1 19970919 | |
| WO 9704109 | A1 19970206 | WO 96-FR1132 19960718 |

W: CA, JP, US
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
CA 2227030 AA 19970206 CA 96-2227030 19960718
EP 842282 EP 19980520 EP 96-926424 19960718
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, NL, SE, MC, PT,
IE, FI

PRIORITY APPLN. INFO.: FR 95-8901 19950721
WO 96-FR1132 19960718

AB Disclosed are recombinant multimeric proteins comprising at least (a) fusion protein A contg. C4 binding protein (***C4BP***) .alpha. chain C-terminal residues 124-549 and a heterologous protein and (b) fusion protein B contg. ***C4BP*** .beta. chain C-terminal residues 120-235 and a heterologous protein, the proteins A and B binding to each other through the C-terminal domains to form the multimeric protein. Recombinant cells producing the multimeric proteins as well as use of the heteromultimers or cells for fetal-maternal alloimmunization, for therapy or prophylaxis of infections, for therapy of autoimmune diseases, for immunotherapy and for diagnosis are also disclosed. Thus, ***anti*** - ***Rh*** (D) scFv- ***C4BP*** and CD43 fragment- ***C4BP*** fusion proteins were produced with CHO cells. The heteromultimeric protein formed agglutinated Rh+ erythrocytes.

L11 ANSWER 2 OF 2 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 1998022791 MEDLINE
DOCUMENT NUMBER: 98022791
TITLE: A recombinant human scFv ***anti*** - ***Rh*** (D) antibody with multiple valences using a C-terminal fragment of C4-binding protein.

AUTHOR: Libhy M T; Goossens D; Oudin S; Gupta N; Derville X;
Juszczak G; Cormillet P; Bougy F; Reveil B; Philbert F; Tabary T; Klatzmann D; Rouger P; Cohen J H
CORPORATE SOURCE: Laboratoire d'Immunologie, UFR Medecine, Pole Biomolecules URCA, Reims, France.
SOURCE: BLOOD, (1997 Nov 15) 90 (10) 3978-83.
Journal code: ABG. ISSN: 0006-4971.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority

Journals; Cancer
Journals
ENTRY MONTH: 199802
ENTRY WEEK: 19980204
AB Monomeric recombinant molecules prove generally unsatisfactory for in vivo use. Most biological systems are indeed multivalent either structurally, associating different chains, or functionally, when cross-linked by their ligands. Mimicking natural molecules for immune intervention implies the need for multimerizing systems to create multivalent molecules capable of interfering with physiological processing. A multivalent ***anti*** - ***Rh*** (D) recombinant protein has been designed by reconstructing the antibody binding site of a human monoclonal ***anti*** - ***Rh*** (D) antibody as a single chain Fv mini antibody, then multimerizing it by inserting at its C-terminal end the C-terminal part of the C4 binding protein (***C4bp***) alpha chain, which is responsible for the octamer multimerization of that molecule. This soluble multivalent recombinant molecule was functional, bound red blood cells (RBCs), agglutinated them, and did not activate complement. This demonstration model opens the way for future in vivo use of multivalent molecules associating antibody valences and other functional molecules for cell targeting, imaging, or removal of cells such as Rh(D)-positive RBCs for preventing Rh alloimmunization.
=> d12 ibib abs 1-4

L12 ANSWER 1 OF 4 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1996:252939 CAPLUS
DOCUMENT NUMBER: 124:286566
TITLE: Human skeletal myoblasts spontaneously activate allogeneic ***complement*** but are resistant to killing
AUTHOR(S): Gasque, Philippe; Morgan, B. Paul; Legoedec, Jocelyne; Chan, Philippe; Fontaine, Marc
CORPORATE SOURCE: Dep. Med. Biochem., Univ. Wales Coll. Med., Cardiff, UK
SOURCE: J. Immunol. (1996), 156(9), 3402-11
CODEN: JOIMAA; ISSN: 0022-1767
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The ***complement*** (C) system has previously been implicated in several diseases of muscle. We here report that human myoblasts or rhabdomyosarcoma cell lines spontaneously activate C through the classical pathway, causing release of anaphylatoxins and coating of myoblasts with opsonic C fragments but without causing cell killing. Survival of myoblasts is a consequence of the abundant expression of the membrane C regulatory mols. MCP and CD59, and neutralization of CD59 renders cells susceptible to C killing. The decay-accelerating factor was expressed at a very low level. Myoblasts and rhabdomyosarcoma lines also abundantly express the fluid-phase regulators Cl-inhibitor, factor H, C4 binding protein, ***S*** - ***protein***, and clusterin and secrete a sol. form of CD59. Expression of membrane and fluid-phase regulators is enhanced by either IFN-gamma. or TNF-alpha.. Although myoblasts resist C killing, spontaneous activation of C on these cells may have important consequences in inflammatory diseases of muscle where the generation of anaphylactic and opsonic fragments with recruit and activate inflammatory cells. C activation on myoblasts may also have consequences for the use of these cells as vehicles for gene delivery. Inhibition of C using sol. ***complement*** receptor I (sCRI) efficiently protected myoblasts from C attack in vitro, and this agent, already being tested in therapy of several C-mediated diseases, might be of value in inflammatory muscle disease and in improving the efficiency of gene delivery.

L12 ANSWER 2 OF 4 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1996:708713 CAPLUS
DOCUMENT NUMBER: 126:6135
TITLE: ***Complement*** regulatory protein expression by a human oligodendrocyte cell line: cytokine regulation and comparison with astrocytes
AUTHOR(S): Gasque, P.; Morgan, B. P.
CORPORATE SOURCE: Dep. of Medical Biochemistry, Tenovus Building, Cardiff, CF4 4XX, UK
SOURCE: Immunology (1996), 89(3), 338-347
CODEN: IMMUAU; ISSN: 0019-2805
PUBLISHER: Blackwell
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Rat oligodendrocytes spontaneously active ***complement*** (C) and lack the C inhibitor CD59. As a consequence, rat oligodendrocytes are susceptible to lysis by autologous C in vitro. Expression of C inhibitors on human oligodendrocytes in vitro and other human glia has yet to be well characterized. We have previously shown expression at the mRNA level of the membrane inhibitors CD59, decay-accelerating factor (DAF); CD55 and membrane cofactor protein (MCP; CD46) in human astrocytes. We here examine the expression of membrane and secreted C inhibitors by the oligodendrocyte cell line, HOG. HOG cells abundantly expressed CD59, assessed at protein and mRNA level, and expressed CAF and MCP, albeit at a lower level. Expression of all three inhibitors was enhanced by incubation with interferon-gamma. or with phorbol ester (PMA). ***Complement*** receptor type I (***CR1*** ; ***CD35***) was neither expressed constitutively nor induced by cytokines. HOG also constitutively secreted C1-inhibitor, ***S*** - ***protein*** and clusterin. Factor H was secreted only after stimulation with cytokines. C4b binding proteins was expressed at a very low level and was detected only at the mRNA level by reversed transcriptase-polymerase chain reaction (RT-PCR). For comparison, astrocyte expression of CD59, DAF, MCP and ***CR1*** was confirmed at the mRNA and protein levels. HOG did not activate C spontaneously, as judged by the lack of deposition of C fragments, and were not lysed by C even after inhibition of CD59 and DAF using specific monoclonal antibodies.

L12 ANSWER 3 OF 4 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1992:649734 CAPLUS
DOCUMENT NUMBER: 117:249734
TITLE: ***Complement*** activation in the follicular light zone of human lymphoid tissues
AUTHOR(S): Yamakawa, M.; Imai, Y.
CORPORATE SOURCE: Sch. Med., Yamagata Univ., Yamagata 990-23, Japan
SOURCE: Immunology (1992), 76(3), 378-84
CODEN: IMMUAU; ISSN: 0019-2805
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A comparative immunohistochem. study of the distribution pattern of ***complement*** components and regulatory proteins within secondary lymphoid follicles was performed by the immunoperoxidase technique. Fifteen lymphoid tissues including appendices, Peyer's patches and tonsils were analyzed. Sixty secondary lymphoid follicles with evident polarity, i.e., the distinct coexistence of a light zone, dark zone and mantle zone in the same lymphoid follicle, were tested with single antibodies. The light zones were consistently immunostained in a dendritic meshwork pattern with all antibodies. The immunostaining patterns were classified into two major groups based on the immunoreactivity of the dark zone. One immunostaining pattern was characterized by no immunostaining of the dark zone to the majority of the antigens. The second group was characterized by a diffusely weak to moderate dendritic meshwork pattern of the dark zone to some immunostaining for C9 (monoclonal), ***S*** - ***protein***, and DF-DRC1, and all immunostaining of ***CR1*** (

CD35), Ber-Mac-DRC (***CD35***), CR2(CD21), and R4/23. All four ***complement*** regulatory proteins were localized by immunoelectron microscopy attached to the cell surface of the cells, including follicular dendritic cells, in the light zone. The data indicate that there is an evident functional difference between the light zone and the dark zone, and that complete activation of the ***complement*** system occurs only in the light zone.

L12 ANSWER 4 OF 4 CAPLUS COPYRIGHT 1999 ACS

ACCESSION NUMBER: 1992:52936 CAPLUS

DOCUMENT NUMBER: 116:52936

TITLE: C4 binding protein fusions with therapeutically useful

proteins

INVENTOR(S): Pasek, Mark P.; Winkler, Gunther; Liu, Theresa R.

PATENT ASSIGNEE(S): Biogen, Inc., USA

SOURCE: PCT Int. Appl., 105 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. |
|------------|------|------|-----------------|
|------------|------|------|-----------------|

| | | | |
|------------|----|---------|----------------------|
| WO 9111461 | A1 | 1990808 | WO 91-US567 19910128 |
|------------|----|---------|----------------------|

W: AU, CA, JP, US

RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE

AU 9173288 A1 1990821 AU 91-73288 19910128

EP 465633 A1 19920115 EP 91-903951 19910128

R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE

JP 04506460 T2 19921112 JP 91-504137 19910128

PRIORITY APPLN. INFO.: US 90-470888 19900126

WO 91-US567 19910128

AB The ***complement*** C4 binding protein (***C4bp***) is used in fusion proteins with therapeutic proteins to ensure targeting of the fusion protein to the blood and to prolong serum half-life. In particular, the short consensus repeats of the N-terminal region are used.

The primary aim is to provide ***CD4*** antigens for use in the

treatment of AIDS. A cDNA for ***C4bp*** was cloned by polymerase chain reaction amplification of the mRNA and subcloned into the animal expression vector pJOD-10. When the cloned gene was expressed in COS-7

cells a heptameric ***C4bp*** of the correct conformation but lacking the ***S*** ***protein*** -binding subunit was produced. Chimeric genes based upon this cDNA and one encoding sol. ***CD4*** antigen

were constructed and expressed in COS-7 cells. The purified fusion

proteins were shown to form multimers and to bind the glycoprotein gp120

of HIV in vitro. Conditioned medium from producer cells prevented syncytia formation by HIV-infected cells.

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FILE 'MEDLINE, JAPIO, BIOSIS, SCISEARCH, CAPLUS, EMBASE' ENTERED AT

16:18:32 ON 25 APR 1999

L1 983 S C4BP

L2 106 S L1 AND (CD4 OR CD8 OR CD16 OR CD35 OR

CR1)

L3 103 S L2 AND (COAGULATION OR COMPLEMENT)

L4 18 S L3 AND ERYTHROCYTE?

L5 1 S L3 AND C TERMINAL

L6 0 S L2 AND RATIO

L7 6 S L1 AND (ANTI-RH OR ANTI RH)

L8 4 S L3 AND S PROTEIN?

L9 46 DUP REM L2 (60 DUPLICATES REMOVED)

L10 8 DUP REM L4 (10 DUPLICATES REMOVED)

L11 2 DUP REM L7 (4 DUPLICATES REMOVED)

L12 4 DUP REM L8 (0 DUPLICATES REMOVED)

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L5 ANSWER 1 OF 1 CAPLUS COPYRIGHT 1999 ACS

ACCESSION NUMBER: 1997:267203 CAPLUS

DOCUMENT NUMBER: 126:250213

TITLE: Recombinant heteromultimeric C4 binding protein fusion

proteins and their use for vaccines, immunotherapy

and

diagnosis

INVENTOR(S): Klatzmann, David; Cohen, Jacques

PATENT ASSIGNEE(S): Universite de Reims Champagne

Ardennes, Fr.;

Universite Pierre et Marie Curie Paris VI

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DOCUMENT TYPE: Patent

LANGUAGE: French

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| PATENT NO. | KIND | DATE | APPLICATION NO. |
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| FR 2736916 | A1 | 19970124 | FR 95-8901 19950721 |
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| FR 2736916 | B1 | 19970919 | |
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| WO 9704109 | A1 | 19970206 | WO 96-FR1132 19960718 |
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RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU,

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| CA 2227030 | AA | 19970206 | CA 96-2227030 19960718 |
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| EP 842282 | A1 | 19980520 | EP 96-926424 19960718 |
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AB Disclosed are recombinant multimeric proteins comprising at least (a)

fusion protein A contg. C4 binding protein (***C4BP***)

.alpha. chain

C - ***terminal*** residues 124-549 and a

heterologous protein

and (b) fusion protein B contg. ***C4BP*** .beta. chain

C -

terminal residues 120-235 and a heterologous protein,

the proteins

A and B binding to each other through the ***C*** -

terminal

domains to form the multimeric protein. Recombinant cells

producing the multimeric proteins as well as use of the heterooligomers or cells

for

fetal-maternal alloimmunization, for therapy or prophylaxis of infections,

for therapy of autoimmune diseases, for immunotherapy and for

diagnosis

are also disclosed. Thus, anti-Rh(D) scFv- ***C4BP*** and

CD43

fragment- ***C4BP*** fusion proteins were produced with

CHO cells. The

heterooligomeric protein formed agglutinated Rh+ erythrocytes.

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